Bulletin on NARCOTICS

Vol. IV, No. 3, JULY-SEPTEMBER 1952

UNITED NATIONS

DEPARTMENT OF SOCIAL AFFAIRS

New York

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Opening of the seventh session of the Commission on Narcotic Drugs

By Guillaume Georges-Picot

Assistant Secretary-General in charge of the Department of Social Affairs

I am happy to greet the Commission on Narcotic Drugs for the first time since I succeeded Mr. Henri Laugier. The Commission is engaged in a task the importance of which was recognized by governments some forty years ago when the first international convention on narcotic drugs was concluded at The Hague. Other agreements on narcotic drugs were concluded under the auspices of the League of Nations, thus setting up national and international control machinery, the need for which is demonstrated by the well-nigh universal participation of States in these instruments. I have followed the development of this machinery with interest, and since I entered upon the duties of Assistant Secretary-General in charge of the Department of Social Affairs, I have had occasion to study in greater detail the work done in this field since the United Nations replaced the League of Nations.

Few problems have so many different aspects — medical, scientific, social, economic, legal, diplomatic and political, to mention only some of them. The search for a solution of the problems arising out of the international control of narcotic drugs therefore calls upon the United Nations and particularly the Economic and Social Council, your Commission and the Secretariat for efforts in many directions but all tending towards the same purpose: the elimination of the abuse of narcotic drugs. The United Nations has already achieved some results in this direction. Thanks to the 1946 Protocol, the Secretary-General has been able to take over the functions of his predecessor at the League of Nations, while the Protocol signed at Paris in 1948, recognizing the developments in the manufacture of drugs which have taken place since 1931, set up machinery making it possible to bring under international control new narcotic drugs to which previous conventions did not apply. These two instruments were concluded and put into force with remarkable speed and a large number of States have already acceded to these two Protocols within a very short space of time. National and international controls of narcotic drugs which were seriously disrupted by the world conflict have been restored to their pre-war level and adapted to new requirements. Only if governments transmit their annual reports regularly and endeavour to make them accurate and complete will the Commission be able to form a true picture of the situation and to take any action that may be necessary. Needless to say, this comment applies equally to the reports of seizures in the illicit traffic.

Mention should be made, in this connexion, of the interesting laboratory work which has been undertaken with a view to perfecting methods for ascertaining the origin of the opium seized in the illicit traffic. Parallel programmes of research organized in a dozen countries under the auspices of the United Nations have already produced promising results.

In obedience to decisions taken by your Commission and by the Economic and Social Council and sanctioned by the General Assembly, the Secretariat publishes a quarterly *Bulletin on Narcotics* containing the latest information on results obtained by governments, the United Nations and organs set up under the international conventions for the control of narcotic drugs and the fight against drug addiction; in addition it publishes technical and scientific papers on narcotic drugs, and articles on legislative and administrative practice in various countries, while a large section is devoted to bibliography.

But these varied activities could not produce really satisfactory results if no thought were given to attacking the very heart of the problem, that is, the limitation of raw materials. No system of regulation, however perfect, can offer a final solution to the problem of narcotic drugs so long as the very source of these substances escapes control. As regards opium, which despite the introduction of synthetic products continues to be the most important raw material, the Economic and Social Council has taken up the question of limiting its production. I shall therefore merely raise two other problems in that connexion which remain to be solved, namely, the question of the coca leaf and that of Indian hemp.

A commission of experts has been sent to Peru and Bolivia to study the effects of the chewing of the coca

leaf and the possibility of limiting its production and controlling its distribution. During the present session you will have an opportunity to examine anew the report submitted by that Commission and thus to throw some light on certain still controversial aspects of the matter. As regards hashish, if it develops habits which may be less harmful than those resulting from the abuse of other drugs, the fact remains that the problem is extremely serious particularly in view of the vast area devoted to its cultivation and of the number of persons using the drug.

This question of raw materials takes on particular importance at this juncture when you are preparing the single convention on narcotic drugs, on which I should now like to make a few comments.

This new treaty, the drafting of which was entrusted by the Economic and Social Council to the Commission at the latter's own request, will constitute, once it has been signed and has entered into force, the ninth in the series of treaties for controlling narcotic drugs concluded by governments in the last forty years. In a general way the eight existing treaties may be said to form the foundation of a new body of law, the purpose of which is to control the production of and international trade in the vitally necessary but dangerous substances we call narcotic drugs. The importance, the extreme usefulness of precedents is a lesson I learned during my diplomatic career, and I find this truth confirmed once more when I see that all the precedents so painstakingly created since 1912 are so to speak codified in the new treaty.

It is particularly gratifying for me to note that as a whole this draft treaty, which has been prepared by the department of the Secretariat recently placed under my charge, follows the tradition of earlier instruments, and although it codifies existing provisions, it leaves any future conference free to create new precedents in this field. I am happy to see from the observations of governments on the draft that this point has not escaped their attention, one of them having written that "in particular the technical and legal conception of the draft convention was noted with appreciation".

As a matter of fact, while it is sometimes difficult to utilize precedents, it is a much more delicate matter to create them. It is possible that present circumstances are not favourable to unduly radical innovations in the control of narcotic drugs and the adoption of the draft single convention would not represent any radical change in the methods of control but would constitute an important step forward in the development of the international administration of treaties on narcotic drugs, and might have certain repercussions in other fields where international co-operation comes into play.

The Commission thus has before it a draft convention to which special importance may be attached and to which I am sure it will devote its most careful attention. I am aware that the consideration of this question will give rise to the expression of divergent opinions and that it will be difficult to reach unanimous agreement on all points; but I am confident that, with the help of all concerned, the work of the Commission will open the way towards further progress.

I shall close on this note of confidence, and extend to you the best wishes of the Secretary-General for the success of your work.

Further considerations on the coca habit in Colombia

By Professor Jorge Bejarano, M.D.

Former Minister of Health, former Vice-President of the Pan-American Sanitary Bureau, Professor at the National University, Member of the National Academy of Medicine and of the New York Academy of Medicine, President of the National Red Cross Society of Colombia

The Bulletin takes pleasure in publishing the authoritative article of Professor Bejarano on the problem of the coca leaf chewing in Colombia, on which he is also preparing a book. This study — which unfortunately could not be included in the Special Number on Coca (Vol. IV, No. 2) — goes back to the origins of the habit and examines all the aspects of the problem — although more particularly in Colombia — which years of experience and active research have made familiar to Professor Bejarano, both as a Minister and as a Professor

> "As everywhere in the Indies, the natives were in the habit of having herbs or roots in their mouths, including the highly-prized herb known as coca, which is grown in many parts of this country."

"Wherever I have travelled in the Indies I have noticed that the native Indians are very fond of holding roots, twigs and herbs in their mouths. In the district round the town of Antiocha some are in the habit of munching small coca plants, and in the provinces of Arma, other herbs; in the provinces of Quimbaya and Ancerma, they cut some twigs from small and tender trees, which are always very green, and chew these twigs unceasingly. In the other villages which belong to the towns of Cali and Popayan they carry some small coca plants in their mouths, as already mentioned, and from some little gourds they add a certain mixture or concoction prepared by them and put the compound in their mouths; they do the same with a certain kind of earth which is like lime. Throughout Peru it was and is the custom to carry this coca in the mouth, and from the morning till they lie down to sleep they carry it, without discarding it. When I asked some Indians why they always had their mouths full of the herb (which they do not eat or use in any other way except to chew it), they said that they hardly felt the pangs of hunger, but were full of strength and energy. I think that it must in some way produce this effect, although it appears to me a vicious habit, and only fit for people like these Indians. This coca is planted in the Andes, from Guamanga to the town of Plata; it grows into small shrubs, and they cultivate it and treat it with great care in order that it may produce leaves, which they call coca, and which are like myrtle. The leaves are dried in the sun, and then put into long and narrow baskets, holding a little more than one *arroba* each, and in the years 1548, 1549 and 1551, such a value was set on this herb or coca in Peru that it is most unlikely that there can be any annual herb or root or fruit so highly prized as this, with the exception of spices, which are a different matter. The taxes for those years — mostly the proceeds of Cuzco, the town of La Paz and the town of Plata — yielded 80,000, 60,000 and 40,000 and 20,000 pesos, largely on account of this coca. And anyone who received a village of Indians for taxation, took as the principal sum taxable the number of baskets of coca harvested. Indeed, they judged property by the quantity of "Trujillo herb" (as it is known) owned. This coca was sold in the mines of Potosí, and they took a great deal more trouble in planting and harvesting the coca leaf than it is worth. But it will never cease to be esteemed. There are men in Spain who have grown wealthy through buying and selling this coca and trading in the Indian markets."

From *Crónicas de la Conquista*
By Pedro Cieza de León, chapter XCVI

"I have always held that in the forest region coca is a homicidal drug because it engenders malnutrition through the suppression of that protective urge which is called hunger."

Máxime Kuczynsky-Godard
Report of the Commission of Enquiry,
E/1666, p. 138

"And the Indian is paid for his labour and goods in coca. The magnanimous gentry do not want the poor to be aware of their own tragedy. Let them die without understanding their pain or their ignorance. Let them have in their mouths the bitter taste of the leaf which paralyses the urge to rebellion. Give them a little artificial happiness. It is better for them to sleep than to

behold the infinite melancholy of that countryside which is like a reflexion of their own age-long racial tragedy."

Anibal Prado

"The Indians have... at least contributed to the establishment of the famous estates."

Salvador Camacho Roldán

In 1943, I submitted a study on the problem of the coca habit in Colombia to the National Academy of Medicine, at Bogotá.

In this second study I shall revert to the same theme and consider the problem from different angles; I shall also discuss the causes of the coca habit and the misleading arguments apparently relied upon by the opponents of the measures which, as Minister of Health, I enacted in 1947 and 1948 but which, I believe, have not been properly enforced since I relinquished my functions with the Ministry. By contrast with the intention underlying the two decrees (which are reproduced in the appropriate section of this article), the social and public health problem of the coca habit, described in all its gravity in my earlier study, still remains, and it is my intention to raise the matter again and to put it in the hands of those who, in Colombia as throughout the continent, are the guardians of the people's physical and mental health.

The following are suitable headings under which to discuss the coca habit:

1. Antiquity of the use of coca.
2. Botanical study of the varieties of the plant which occur in Colombia; geographical distribution of the plant.
3. Physiological effects of coca.
4. Causes of the spread and continuance of the coca habit in Colombia; its present economic consequences.
5. Measures enacted in Colombia and their results.
6. Map of the Cauca regions where coca is cultivated and chewed, with a rough estimate of the population using it.
7. Co-ordination of agencies in the campaign against the coca habit.

CHAPTER I

Antiquity of the use of coca in Colombia

Although we are told in a beautiful legend that Manco Capac, the ancestor of the powerful Inca tribe, whose vast empire, with its laws and structure, has remained a marvel to this day, and his wife Mama Ocllo, introduced agriculture into their vast dominions and that they made a present of the coca plant to the Indians, who describe it as "driving away hunger and weariness and dispelling sadness", there is evidence suggesting that before the time of the Incas, coca was known to the Arhuacos, whose country is thought to have been in the north-west of South America, possibly in Guiana or perhaps in what is now Colombia. Coca occurred widely in this region of America, particularly in the areas dominated by the Chibchas. From a good many circumstances it is assumed that the Chibchas, when they drove out the Arhuacos, learnt the use of coca from them, and that the Arhuacos, in their flight to the uplands of Bolivia and Peru, introduced the plant and the habit of chewing the leaf in these parts, for the oldest tribe there, that of the Urus, spoke a language which had many affinities with that of the Arhuacos. It is certain that the Aymarás, the Quechuas and the Chibchas, as they expanded, carried coca to the south and the north. Beyond any doubt, the tribes as far north as Panama, and the Caribes, contracted the vice from the Chibchas.

In the countless legends which explain the appearance of coca on earth a divine origin is claimed for coca. One relates that the gods revealed to Manco Capac the existence and magical properties of coca. Another legend avers that coca sprang from the dead body of a courtesan — clear evidence of its original use as an aphrodisiac. There are still some tribes in Colombia which, like the Kogi or Cábaga, a small Indian community living in the Sierra Nevada de Santa Marta, preserve the tradition that coca promotes fertility, at least during the early years of the habit, when the sexual instinct is stimulated, although later it declines and impotence supervenes, as is proved by the physiological action of cocaine.

The rationalization of the effect of coca on sexual activity has certain exceptional characteristics in this tribe, according to Dr. Gerardo Reichel-Dolmatoff, Director of the Magdalena Ethnological Institute. These characteristics would offer ample scope for the observation and theories of psycho-analysts. The ideal of life, in the Kogi culture, is to eat nothing but coca, to abstain from sexual intercourse, never to sleep, and to speak of the "ancients", i.e., to sing, dance and recite. The coca is the miraculous plant which helps man to achieve this ideal. The ceremony at which young men are initiated in the coca habit is marked by a complex symbolism. The young man receives the small gourd of lime with which the coca he chews will be mixed, and he is made to understand that the small receptacle represents a woman. The young man is married to this woman during the ceremony, and perforates the gourd in imitation of the ritual deflowering, The small twig with which he does this symbolizes the penis. The introduction of the twig into the small gourd or receptacle and the gesture of rubbing round the opening, are interpreted as the symbolizing of the sexual act, and in their culture this means that all sexual intercourse is

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to be abandoned, its only manifestation or expression being the symbolic use of coca. Thus, the whole life of the Kogi, their entire immense frustration, is concentrated on this small object, which represents the reduction of their mortified desires into the elementary trilogy "woman", "food" and "memory" (*Los Kogi, una tribu de la Sierra Nevada de Santa Marta,* by G. Reichel-Dolmatoff; pub. Iqueima, 1951).

In the remains of the civilization of San Agustin, as represented by its statues, there is unmistakable evidence of the use of coca, as revealed by the innumerable statues which have been studied by Colombian and foreign ethnologists and anthropologists. Preuss, José Pérez de Barrada, Sergio Elías Ortíz, have all suggested that the clearly marked circular protuberances which are observable in the cheeks of many of the statues from San Agustin, are without doubt intended to represent the quid of coca which was being chewed and held in the mouth.

Other sculptures dating from the heyday of the Agustinian culture, about the third century A.D., and representing warriors or tutelary deities, depict figures in the act of ejecting something which is assumed by these authorities to be a wad of coca leaf. They think that these statues probably represent a deity to whom the use of coca was consecrated.

Professor K. Th. Preuss, who has written some very fine studies of the statues and monuments of San Agustín in the department of Huila, reports that many of those studied by him were marked by bulges or protuberances in the cheeks, which he could only interpret as depictions of the coca-leaf chewing habit.

The San Agustín culture has been proved to antedate the great migration of the Chibcha peoples, which originated in the Isthmus of Panama not before the seventh century A.D. Hence, says Pérez de Barrada, the idea that the coca habit spread from the north to south is not tenable.

But the true origin of the coca leaf chewing habit is apparently lost in the mists of time. Even the etymology of the name "coca" — or the other names by which it is known, "ipadá" in the department of Amazonas, "cuca" in Quechua, "hayo" in Brazil and Venezuela— is obscure. Vinelli and Nuñez del Prado trace it to the Aymará term for "tree" which, they say, means anything in the vegetable kingdom. Nuñez del Prado thinks it is a proper name symbolizing the benign properties ascribed to the leaf from time immemorial. Some think that the word "coca" means "food", which would be in accordance with the belief that it was a foodstuff.

As Dr. Ramón Pardal observes in his *Medicina aborigen Americana,* the Indians of America, like some other native peoples, had and still have the habit of ingesting or absorbing vegetable substances of an alkaloid character and intoxicating effect.

No research can ascertain how it came about that each region was endowed by nature with the plant which was to be put to such uses. Clearly, however, the method of use, or the similarity in the technique employed to produce the best results, is a vestige of the habits of other peoples, so that even a person who is not an ethnologist is led inevitably to conclude that this is an imported custom spread by the migration of peoples. The chewing of coca, mixed with other substances to release the alkaloid content of the leaves, is exactly similar to the custom of the ancient Malays, Polynesians and Indonesians, who chewed betel leaves (betel being a creeper of the genus *Piperaceae*), also with the addition of an alkali. From the ethnological point of view, this fact is of inestimable value in establishing certain basic points concerning the origins of the peoples of South America.

Nor is it possible to determine precisely when coca made its appearance in South America. There is evidence that it existed in pre-Inca days, but it has hitherto been impossible to establish how long before the Inca period this plant, which was to exercise so great and so harmful an effect on the original inhabitants of South America, began to enjoy its vogue. Historians are, however, unanimously agreed that the great Inca Empire was built up and attained its magnificent pre-Hispanic cultural apogee some time before coca addiction had begun to produce its now familiar ravages. Something similar occurred in the case of *chicha,* which certainly accounts largely for the decadence of the Chibcha culture.

According to many chroniclers of the period, Amerigo Vespucci was the first to bring reports of the use of coca back to Europe. In a letter attributed to him, he writes to Duke René II, of Lorraine, that "at the mouth of the River Pará or Amazon I found that all the Indians had their mouths filled with a certain green herb which they munched, almost like animals, so that they could hardly utter a word". The famous navigator goes on to describe in this letter the little gourds in which the Indians carried the lime, which, according to him, was like "ground chalk". According to other sources it was the monk Tomás Ortíz who, on his return from America, first brought reports of the coca back to Europe.

Actually, the old world did not see the leaf itself until 1750, when it was brought to Europe by the naturalist Joseph de Jussieu, and it was not until a century later (1859) that Nieman, in the course of his research leading to the discovery of cocaine, demonstrated how the coca leaf acted, a chemical process which had been used, empirically, from far distant times by the peoples of the Andes. It appears clearly proved that the coca plant originated in South America. Maier states, though no source of information is given, that the coca was cultivated only in the gardens of the Inca, and the seeds would presumably have been carried

to distant places by the birds. Nowadays coca occurs in the West Indies, Ceylon and Java.

I have not been able to trace through any document the historical or other source from which the Indians learnt that the chewing of the coca leaf with the addition of an alkali released the alkaloid which Nieman only succeeded in isolating in 1859, in connexion with his discovery of cocaine. This is something which ought to be verified, because, from a scientific and impartial point of view, the significance of the phenomenon is this: a chemical process which was not discovered by civilized man until a century ago had for long been known to these primitive peoples — a circumstance, surely, that bespeaks a high level of culture. Further, it is a fact that coca was used in the Inca Empire not only for chewing, but as an important element in therapy among the Indians. In his fine medical and social study on the coca in Inca Peru, Luis N. Sáenz states that there is conclusive evidence that cocaine was used as a local anaesthetic in operations such as trepanning. It is well known—and it is still remembered in the medical profession—that in the Colonial and Republican periods coca was put to many medicinal uses. The supposed aphrodisiac properties of coca are still in demand among the highlanders of Peru, who believe that coca preserves virility until late in life. Coca is still used as an ingredient in magic philtres and potions, and as a dentifrice.

CHAPTER II

Geographical distribution of the coca plant in Colombia

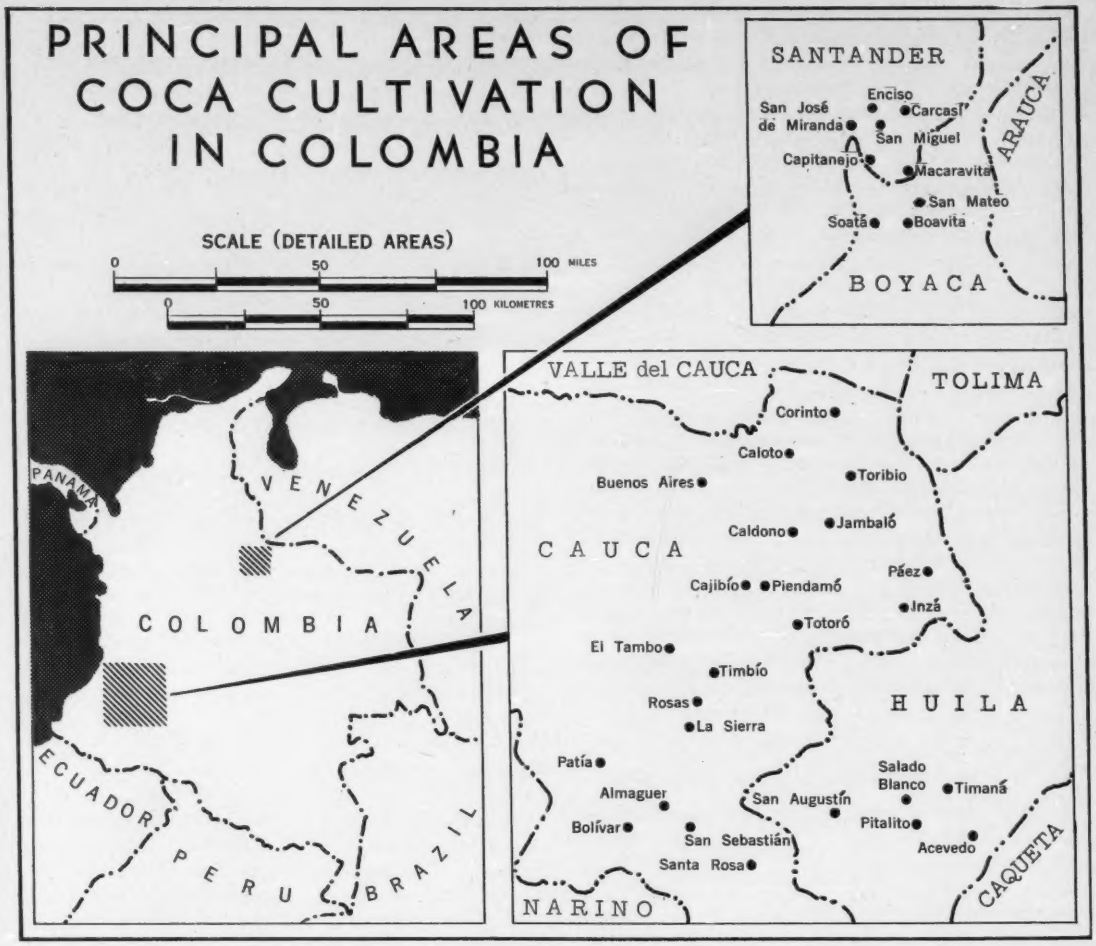
We know that the habitat of *Erythroxylon coca* (red wood) is in the valleys of the Andes, in the uplands of warm countries and in latitudes where the days are short. The botanist Sauer, in his *Cultivated Plants of South and Central America,* noted that its oecology appears to be similar to that of the cocoa tree, although, in their value to man, the two plants are quite distinct. According to this author, coca seems to have been grown exclusively in a large area in the west and northwest of South America, bounded on the north by the coca-tree belt and on the south and east by the tobacco belt. Suitable temperatures range from 16° to 24°C, with a humid atmosphere and a sandy soil which is not damp or swampy.

Coca is not now cultivated outside the departments of Cauca, Huila, Boyacá and Santander del Sur, being grown chiefly in the first two, for in Santander it is confined to the municipalities of Capitanejo, San Miguel and Macaravita, and in Boyacá to those of Boavita, San Mateo and Soatá, whereas, in Cauca it is grown in the following twenty municipalities:

Of course, neither the cultivation of *Erythroxylon coca* nor the habit of chewing the leaves is limited strictly to the departments mentioned. The Amazonian region of Colombia has also been invaded by the vice, as we know in detail from the publications of many research workers and missionaries, including Fr. Marcelino Castellvi, who was unfortunately lost to science a short time ago.

From such reports it may be gathered that coca is used in the following old or modern coca areas in Colombia, so far as these are now known: Goajira, Costa Atlántica, Magdalena, Norte de Santander (amongst the *motilones*), Santander del Sur, Boyacá and Cundinamarca (old area), Cauca, Huila, Nariño. Amongst the tribes of the department of Amazonas, mention should be made of the Rossígaro, the Yukuna,

Municipality	*Hectares under cultivation*	*No. of trees*	*Production in kg.*
DEPARTMENT OF CAUCA			
Almaguer	100	3,000	29,800
Bolívar	20	2,500	10,800
Páez	60	2,000	1,200
Buenos Aires	2	1,200	800
Cajibio	2	1,240	900
Caldono	2	1,260	1,000
Caloto	15	2,300	1,500
Corinto	15	3,000	8,400
El Tambo	—	6,025	—
Patía	10	1,300	1,500
Inzá	30	2,500	15,600
Jambaló	17	2,000	—
La Sierra	32	—	—
Piendamó	1	500	180
Rosas	1	—	140
San Sebastián	20	2,000	10,800
Santa Rosa	1	1,500	720
Timbio	10	2,500	5,820
Toribio	4	2,000	2,400
Totoró	25	2,600	12,000
	367	39,425	103,560
DEPARTMENT OF HUILA			
San Agustín	400	60,000	30,500
Pitalito	—	42,000	47,000
Acevedo	—	5,000	4,200
Salado Blanco	—	3,000	1,500
Timaná	—	100	—
	400	110,100	83,200
DEPARTMENT OF SANTANDER			
Capitanejo	—	60,000	—
San Miguel	—	15,000	—
Macaravita	—	18,000	—
San José de Miranda	—	10,000	—
Enciso	—	12,000	—
Carcasi	—	10,000	—
		125,000	
DEPARTMENT OF BOYACÁ			
Boavita	—	800	60
San Mateo	—	1,000	90
Soatá	—	700	50
		2,500	200
SUMMARY			
Cauca	367	39,425	103,560
Huila	400	110,100	83,200
Santander	—	125,000	—
Boyacá	—	2,500	200
GRAND TOTAL	767	277,025	186,960



and the Mirañas; and in the department of Putumayo there are the Huitotos and also the Kofan.

So much for the geography of the plant. The fact which cannot be ignored is that the coca habit originated in the Inca Empire, from which it spread after the Inca conquest to the peoples who lived in the areas which later became Greater Colombia. However, Dr. Luis A. León, in his interesting study *El cocaísmo en el Ecuador,* puts forward the theory that the vice was native to the sister country, basing his view on archaeological finds in the Carchi area, where statues were discovered which represent human figures in whose cheeks can be seen the swellings reminiscent of the leaves held in that position.

Golden Mortimer, the United States archaeologist, in his book *Peru, History of Coca, the Divine Plant of the Incas,* indicates the following possible route for cocaism on its journey northward. The Kingdom of Quito after its conquest by Tupac Inca Yupangui, became part of the great Inca Empire. On the death of this monarch, he was succeeded on the throne by Huaimacapac, who was succeeded in his turn as lord and master of the Kingdom of Quito by his son Atahualpa. The wealth and culture of the Kingdom rivalled that of Peru. The author concludes, "it therefore seems quite probable that as the interests of the government extended northward the customs of the people of the lower Andes should follow, and be propagated among a people where similar conditions called for whatever beneficial influence might be derived from the use of coca. From Quito travel northward, aided by the canoe navigation of the Cauca and Magdalena rivers, would rapidly carry the customs of the people of the south to the northern coast, where, as shown by early historical

facts, commerce was so extensive as to favour the adoption of the habits of the interior".

But the small areas where coca was grown were to be extended after the discovery of America and the Conquest, since all who have studied the historical and sociological aspects of the coca are agreed in admitting that, under Spanish rule, the vice or habit increased on a gigantic scale as the result of efforts to dominate the Indian economy. Furthermore, the trade in coca was a highly profitable business venture and yielded fabulous profits, as all, from the Inca Garcilaso de la Vega to the chroniclers and monks who came to America after its discovery, have testified.

We have yet to find out the obscure reasons why the vice should have remained confined to the areas where the cultivation of the plant was originally known, for at least in Colombia the plant can be grown in regions much lower and warmer than those where it is traditionally known. Besides, man shows remarkable ingenuity and resourcefulness in spreading in all environments anything relating to vice or the depravation of morals. Some authors incline to the explanation that precisely because coca was reputed to relieve fatigue and to invigorate, the inhabitants or workers who had to earn their livelihood in high altitudes like the *páramos* contracted the habit. But this does not, in my opinion, explain why the vice failed to spread to regions where geographical and working conditions were such as to favour the spread of the coca habit.

CHAPTER III

The physiological effects of coca

A social hygiene campaign must be based entirely upon scientific and sociological evidence of the perils of addiction or habituation to substances injurious to the human organism. It is, for instance, impossible to accept the mere statement formerly made in Colombia by laymen, and even by doctors, that *chicha* was a healthy drink and a food substitute essential to the worker in the regions where it was traditionally consumed, when that conclusion was not supported by any clinical or analytical study and did not take into account the simple objective observation that addicts who gave up the habit, so far from showing signs of undernourishment or other deficiency, made impressive recoveries ranging from psychological rehabilitation to improved nourishment; this is all the more true in the case of a campaign which involves problems that medicine and hygiene have to solve, since both rely on the scientific and experimental method.

In the case of the coca and other deleterious habits, traditional empirical assumptions have always predominated. The fact that the vice was confined to certain regions in which the worker manifestly performs a day's work or climbs great heights without needing any sustenance other than two or three handfuls of coca leaves to chew convinced both the indigenous inhabitants and the Conquistadors that coca was a food, a tonic for the heart and endowed with marvellous restorative powers.

This physiological effect has always struck me as the most plausible justification for the use of coca; this is the effect which has invariably impressed laymen and scientists alike, as well as business men and soldiers who, like Miller, a participant in the struggle for South American independence, believed that their troops' stamina was due to the fact that they chewed coca. The scientific explanation for the phenomenon is that, in dispelling fatigue, coca affects the sensory perceptive centres and blurs the sense of time, so that the person under its influence believes that time passes more rapidly than it does. These factors increase the efficiency of muscular work and disguise the feeling of fatigue.

Sáenz and his collaborators ascribe the artificial energy and stimulation due to coca chewing to the changes it produces in the metabolism. He and other authors have demonstrated that the clinical measurement of coca chewers' metabolism shows striking differences, according to whether the test was made when the subject was under the influence of coca or was made long before or after. If Pretti and Sáenz are correct in their observation that the metabolic rate of chewers who have given up the habit is appreciably slower, this would account for the intellectual impairment, under-nourishment and other abnormalities found in addicts. The reduction in the metabolism which occurs with the withdrawal of coca, they state, would be analogous to the paralysis of all the functions stimulated by coca, due either to prolonged addiction or to deprivation.

However, perhaps coca owes most of the esteem in which it has been held since the earliest times to its reputed powers of sexual stimulation. There are hints and glimpses of the aphrodisiac effect of coca in the legends explaining the plant's appearance on earth which were current among the indigenous inhabitants. This effect is as clearly established as that of cocaine, which was formerly mistakenly thought to possess anaphrodisiac properties. All addicts attest this; many elderly coca chewers attribute to coca the fact that their sexual prowess is as great as it was in their youth.

The influence of coca on the sexual activity of the indigenous inhabitants is also noted by Dr. Hermilio Valdizán in his interesting studies of mental disease among the Peruvian primitives, whose hyper-erotism he ascribes to the influence of coca. Seminario Helguera links the abnormal and perverted sexuality of the inmates of the Lima gaols to the high rate of coca consumption among prisoners.

These and other aberrations of the sexual instinct resulting from the use of coca, such as homosexuality and bestiality, have been so common and obvious that they have been noticed even by persons without medical knowledge or specialized acquaintance with these

matters. The vivid narratives of the chroniclers of the Conquest are full of accounts of sodomitic, homosexual and bestial perversion. In the description of historians of three or four centuries ago we find accounts of the same abnormalities which today are part of the classic depiction drawn by authors who have studied the symptoms of cocaine addiction. Coca owes this magical effect, perhaps the most attractive of all to primitive man, to the action of the cocaine alkaloid, a stimulant to all the vegetative functions; but ultimately it degenerates into the most degrading manifestations.

Is coca a food? Like other green leaves, vegetables and fruits, the coca leaf has been found to contain a considerable quantity of the vitamins best known hitherto, particularly B1, B2 and C. What, then, accounts for its apparent quality as a substitute for the need for food? Possibly its high vitamin content offers a clue. If so, ought we not to conclude that the coca habit would be sufficiently vindicated?

Many factors contribute to the misconception that coca is a substitute for food.

The first is, perhaps, the anorexia of addicts. Anorexia is a symptom common to all drug addiction. The only difference is that in the case of coca this deleterious effect has usually been singled out for admiration and praise among all the "marvellous effects of the divine plant". The loss of appetite due to drug addiction has even suggested a method of silencing revolt and popular disturbances caused by the hunger of great masses: recourse to the ignoble expedient of making them addicts to such drugs as opium.

Anaesthesia of the mouth, however, also plays a part in coca-induced anorexia; the sense of taste disappears, which explains only too well the rudimentary cookery of addicts. To this must be added the lesions, such as the burns on the mucous membrane caused by the lime, so commonly observed among chewers; ulceration and subsequent scarring leave congestions of the mucous membrane which dull the sensitivity and cause the "toad-mouth" of addicts observed and described by López Albújar. The anaesthetic action of coca, or rather of the alkaloid released in this chemical process, thus fully explains the suppression of the sensations of hunger and thirst.

Accordingly, there is no real evidence that coca has any nutritive value, and, even if it had, there would be no justification whatever for authorizing the use or habit of coca chewing, since countless other sources of vitamins, in no way dangerous to man, are readily available, such as fruit, many varieties of which are to be found and are easily grown precisely in the climates and regions in which the vice is prevalent.

The impairment of sensitivity affects not only the mucous membrane of the mouth, tongue and stomach but also, apparently, the eye and the pharynx. Medical experts both in Peru and in Bolivia note the disappearance of the pharyngal reflex in coca chewers and the stoicism with which they bear such painful afflictions as corneal ulcers and iritis.

Medical practitioners in centres and regions where there is coca addiction note the general dulling of sensitivity in addicts. Many claim that this hypoaesthesia is characteristic of the indigenous inhabitant, and many, like Valdizán, go so far as to advance this as an explanation of the stoicism with which that race bears painful afflictions or such physiological acts as giving birth, which persons of other races make an occasion for highly emotional displays. Professor Edmundo Escomel has even stated that this deadening of the general sensitivity is not merely personal, but may well be hereditary. Yet, I am inclined to agree with Luis M. Sáenz that not enough information is as yet available for any definitive conclusions to be drawn with regard to racial characteristics.

Once the empirical notion and the legend that coca is a food or an antidote to fatigue are refuted, those who want to justify the use of coca fall back upon the contention that the coca leaf is useful or necessary for the life of the Andean man. The great authority of Professor Carlos Monge has been instrumental in inventing and popularizing this thesis, obviously incorrect though it is. The belief has grown that coca contains some element — cocaine or something else — which either helps man to adapt himself to great heights, adds something to the deficient nutritive value of food or increases the efficiency of muscular activity at heights above 2,500 metres.

Pages could be filled with the arguments and examples which disprove this theory. One need only observe that very active workers, who are thoroughly adapted to their environment but do not have the coca habit, are to be found at great heights. The white immigrant and the *mestizo* born in the region do not need to chew coca in order to work or stand the height. They are superior in weight and strength to the Indian chewer. Finally — and this argument is irrefutable — there are regions in Colombia no more than 800 metres in altitude where coca is chewed, and very many other regions much higher than 2,500 metres where coca addiction has never been known, either among the indigenous inhabitants or among immigrants. Observation of the Peruvian and Bolivian armies, both, and especially the latter, composed largely of Indians, shows that the suppression and prohibition of coca chewing does not reduce physical capacity one whit. On the contrary, all military observers point out that deprivation of the leaf improves the men physically and mentally.

Hence there is no scientific evidence for the contention that the Indian differs physiologically from other men, that he needs a pseudo-stimulant in order to adapt himself to living in the highlands, or that he has any special racial attributes that enable him to tolerate cocaine, a substance which is invariably harmful to the human organism. The true explanation is, I think, that

it is the wretched life and environment of the coca addict that lead him instinctively to coca for the alleviation of his woes, and that there is no connexion whatever between the vice, the race and great height. No one can dispute or deny the fact that the coca habit has been and still is a phenomenon due to the economic and social circumstances of large sections of the population of Colombia, Bolivia, Peru and Argentina. César Uribe Piedrahita states in his *Esquema para un estudio de la patología indígena en Colombia:*

> "The reason why the habit of chewing the coca leaf is so widespread among the natives in the south of Colombia can be easily explained. In reality this vice is promoted by the landholders; a great part of the daily wage is paid in coca . . . It is also easy to explain the route taken by coca along the mountain ranges and great rivers where the autochthonous races received from their brothers from the south and from foreign masters this deplorable custom so destructive of ambition and life".

The reaction of coca addiction on the subject's psychological state closely follows the changes it makes in his feeding and in such organs as the ductless glands. Many of these reactions are clearly reflected on the subject's features at the moment when the cocaine is liberated and absorbed. I described them in the first study I made some years ago, and the relevant passages may profitably be quoted in this context.

As soon as the cocaine is released and begins to invade the organism, the subject has an agreeable feeling of euphoria and joy. The breathing becomes deeper; the nerves and heart are stimulated; the muscles seem to be invigorated; the eye brightens; and everything about the subject seems to indicate a greater propensity to work. That is why the Indian feels very restless; he gets up and walks about, seizes his tools, especially the *machete*, and sets about his work with an enthusiasm which might almost be said to verge on frenzy. All who have witnessed the foregoing scene agree that this unaccustomed activity is carried to such extremes that the subject in this state may be a danger to his mates working beside him, for he fells trees or wields his *machete* without the slightest regard for his fellow-workers. This may well be the cause of the accidents which so frequently befall subjects and those working with them. This display of muscular energy is the result of the euphoria and optimism which flood the intoxicated subject's entire organism and border on megalomania, since he believes himself to be the owner of the land he is working, of the flocks and herds around him and of the countryside as far as the eye can see. Two hours later, the pleasurable intoxication has evaporated and the Indian once again becomes aware of his true condition; he realizes once more how utterly wretched he is; the spectre of apathy and ancestral woe once more overshadows his feckless existence. Another chew, and the same joyous sensation that began the long day fills him again, and so the vice goes on indefinitely.

Many of the most striking psychological symptoms and impairments observed in the native coca addict are also common to most forms of drug addiction; indifference to economic problems, for example, and lack of ambition and aspirations.

Sáenz states that the part played by coca in the etiology of mental diseases among descendants of addicts has not been clearly established. Valdizán accepted it, basing himself on the character deterioration and the oligophreny which he and Krumdieck claim to have observed in the descendants of coca addicts. Knowledge of these matters is even more scanty in Colombia than in Peru, for despite the prevalence of the vice, the authors are silent about this aspect.

On the basis of these effects on the subject's psychology, the abnormalities in behaviour, the reluctance in acquiring education and the low level of intelligence observed in coca addicts, physiological inferiority has sometimes been identified with the incurable racial inferiority, which, I think, may be compared with that formerly ascribed to those whose indulgence in *chicha* went back for centuries. All of us recall how contemptuously the rural inhabitants and workers of Boyacá and Cundinamarca were treated, who used to be regarded as inferior beings, almost as intermediate between man and beast.

But there is no such thing as this racial inferiority. The real truth is that various factors — which can be eliminated — cause ethnic groups to appear inferior, particularly when compared with racially similar groups.

But, disregarding such factors as drug addiction, similar or kindred ethnic groups differ widely in mentality and psychology according to whether they do or do not adjust themselves to the influence of their environment. Compare the negroes scattered throughout the world, those, for example in Colombia or in Africa, with those born and brought up in the United States. Their innumerable banks, loan corporations, insurance companies, co-operative societies, their thousands of schools, several universities, many scientists, including more than two thousand physicians and surgeons, their uncounted artists and men of letters attest to the mental and cultural capacity of those who were once slaves and beasts of burden. Thus, there is no such thing as an inferior man or race; the assertion of German philosophers is untrue.

If there is one form of drug addiction which could have caused final bankruptcy of a race's spiritual and cultural values and which not only has prevented any attempt at regeneration, such as the search for means of improving its condition, but rather has plunged it yet further into servitude and completely eradicated any urge to rebellion, it is addiction to cocaine; for it leads to malnutrition, to unhealthy and rudimentary housing, to a dulling of the emotions, to mistrust, to irascibility

and to that propensity to lying and slander which is so typical of vice-ridden groups.

Although no study has as yet been made of the character of the groups in Colombia which have consumed coca from time immemorial, there can be no doubt that lingering drug addiction, affecting the vegetative and endocrinal systems and influencing the sensory and motor systems must inevitably affect what Bowen, in his magnificent work on character, calls "dispositions". If coca addiction, like all drug addiction, reacts on the intelligence, sociability and personality — three attributes of character — it is bound also to alter the traits and lineaments of the character. The Ministry of Health or the Ministry of Education should order some such study to be prepared, for it would, besides, be invaluable from the purely ethnic and social point of view.

Similarly, no research has been done into the relationship between delinquency and coca addiction. We know nothing whatever about the life of the coca addict nor about the drug's influence as manifested in anti-social behaviour. But the studies and observations made by the Peruvian physicians definitely suggest that coca addiction predisposes to crime, a fact which is not only shown by the greater prevalence of crime in the highlands than in the coastal region of Peru, but is also amply borne out by the physiological effects of cocaine, which tends to aggravate existing psychopathic disorders and to precipitate criminal outbursts. If we add the action of *aguardiente* or rum, intoxicants which the State itself popularizes, we have ample evidence for regarding the rural coca addict as a potential or actual criminal. The Ministries of Health and Education might well supplement the study on character suggested above by one on the incidence of crime among coca addicts.

CHAPTER IV

Causes of the spread and continuance of the coca habit in Colombia, and its present economic consequences

No serious student of the coca habit has failed to recognize that the vice has been extended and maintained by interested parties. In the case of coca, we inherit from the Conquest and colonial era the desire for mastery over the indigenous economy, by any methods, a circumstance which affected employment and the remuneration in money or in kind which was paid for it.

This is not a groundless statement. Like *chicha,* a drink reserved for the nobility and the priests, coca was also a privilege of the upper classes and the priesthood. This is amply supported by evidence and borne out by the most trustworthy and authentic historic documents, which show the extent to which the Indian was down-trodden, exploited and oppressed, by the plundering of his land and the system of servitude, disguised under such names as *encomiendas, obrajes, pungucaje, mitanaje,* and *servicio personal.* All this, it is only fair to recognize, in spite of the legislation passed by the Spanish Crown, which vainly endeavoured to pursue a humanitarian colonization policy and also in spite of the spirit of priests such as Fray Bartolomé de las Casas, who, with many others, fought for the recognition of the indigenous peoples—still in our own times contemptuously referred to as "savage peoples" or more briefly "Indians" (*indios*)— as persons with an individuality and culture of their own.

Fray Bartolomé de las Casas, like many other priests imbued with Christian philosophy, fought not only against the abuses of the Conquistadors, but also against the "physical subjection of the indigenous peoples". The infamous application of the policy of force, which only served to destroy the very elements of colonization, as it was Indian labour which cultivated the land and worked the mines, did not entirely disappear with the Republic nor can it even now be said to have been entirely eradicated. There are still many countries in America where the indigenous communities are the victims of that anti-Christian system. Even if the evil policy of force is no longer applied, there still remains the policy of rule through coca, which in the last analysis is nothing more nor less than enslavement of the worker and his economic situation with a view to getting every ounce of physical energy out of him in return for very low wages.

With the aid of drug addiction, men have sought to achieve not only the economic servitude but also the total submission of the peoples they wished to govern. History is full of examples of this. Legrain relates that opium subjugated the Chinese and that a powerful nation made war upon them to impose its use; that, in America, settlers used alcohol to aid them in overcoming the redskins; that the Swedish people also used it to conquer the Laplanders and the French to subjugate the African negroes. *Chicha* was also an instrument in the domination of the Indian peoples by the Spaniards. In the opinion of Sáenz, coca was a valuable aid which the Spaniards knew how to utilize in their conquests. He further states that the Indian who used coca for its medicinal value and mythological significance, upon discovering its narcotic properties, surrendered himself to the vice, thus signing his own slavery sentence for a period which is not yet at an end, and from that sentence neither independence nor the laws which have been passed on his behalf have yet been able to free him. Authoritative historians state that drug addiction contributed to the final disappearance of the Inca people, which once numbered eighteen millions and was later reduce to one million, and that it too played a part in the disintegration of the fascinating Inca culture.

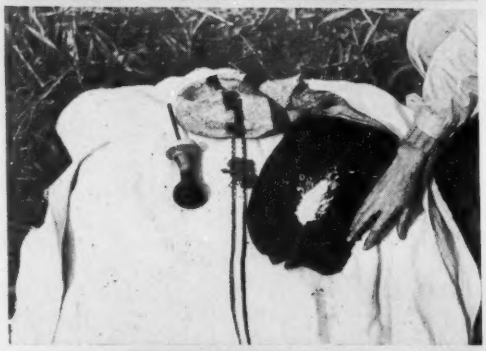
As Sáenz states in his excellent work on the coca leaf in Peru, and as so many others have written, the hour of real independence has not yet come for the Indian coca-chewer. It is a fact that the mental and intellectual standard of these poor people, living in

THE OLD AND THE YOUNG. Above are two typical Indian women from the Sierra region of Colombia. Women do not habitually chew the coca leaf and, therefore, do not show the characteristic lesions caused by this habit.

Colombian Coquero

In the two picture strips on the right and on the facing page, a *coquero* shows how he prepares and stores the lime that he will use in chewing the coca leaves.

The lime, mixed with the coca leaves, permits the release of the alkaloids of the plant and facilitates their absorption by the body. It is extremely interesting to note that without, of course, any theoretical knowledge of chemistry, these primitive people found out, centuries ago, a process which is perfectly efficient for bringing about the extraction of those alkaloids. This is one of the mysteries that ethnologists have not yet been able to solve. Since the hypothesis of trial and error must be considered unlikely and since the thesis of any-



body arriving at that method purely at random is equally unlikely, the mystery remains.

First he gathers and splits wood for the fire. A few sticks generally suffice, and on these are placed the shells that will calcinate and thereby produce the lime.

The lime is then gathered from the fire and placed in a mortar, where it is ground to a fine powder. It is then put in a calabash gourd, which the *coquero* closes by means of a small sharp stick of hard wood. He uses the calabash gourd, such as displayed, as a container in which he carries the lime.

In the next photograph, he picks up a small lump which he pushes inside the ball of half-chewed coca leaves.

Typical landscape in the Colombian sierra.

enslavement to the drug, not only makes them unfit to assimilate the manifold benefits which civilization and culture have brought to Colombia, but even prevents them from enjoying the very small advantages available to those Colombians and foreigners who, though living in the areas where the vice is prevalent, nevertheless keep free of it.

Colombia, more than any other country, provides evidence of the fact that the survival of the habit is due to the ambition to control the indigenous economy, which is characterized by extremely low wages and by excessively long hours of work. It is traditional, and forms part of our idea of the Indian, that as a worker it should be considered his lot to perform work which would not be expected of any other race.

But in view of the deep-rooted influence of coca among the indigenous peoples and the part it has played in Indian sociology, it seems likely that the supression of drug addiction would produce fundamental changes in them, which, in my opinion, would have striking results in the economic field, reflected in agriculture, stock-raising and industry generally. A similar phenomenon has been observed in Cundinamarca and Boyacá since the abolition of *chicha* and *guarapo,* and is readily understandable when it is realized that what is involved is the incorporation into the national economy of quite large groups or communities which, in the case of those who drank *chicha,* were almost non-consumers of food, clothing and other necessities, as they existed almost entirely without them. Obviously this transformation will not take place without involving substantial economic reforms or consequences, one of them being that the Indian, when he is aroused from his stupor and no longer views the world from the artificial paradise of the "miraculous drug", will cease to exhibit that indifference to money and that apathy which are the common marks of all drug addicts.

Finally there is one incontrovertible proof that coca addiction persists in Colombia for reasons which have nothing to do with the Indian. Whereas in Bolivia and Peru *Erythroxylon* is cultivated to supply a genuine agricultural industry connected with the export of coca, an industry which yields many thousands of pesos, in Colombia it is grown exclusively for local consumption. So we have land suitable for food crops for human beings or animals, devoted to the useless cultivation of a plant for which there is no justification whatsoever and which should have disappeared many years ago. It can therefore be concluded that with coca, as with *chicha,* economic reasons rather than myths and legends have provided the most solid foundation for its survival up to our own day and have been its best ally in the efforts to perpetuate a genuine form of drug addiction. The situation is all the more reprehensible in that the habit affects exclusively Colombia's small groups of Indians, humble ignorant people who should be looked after with the greatest care, as our best human reserves and the remains of a race which can trace its ancestry back to the origins of our country.

CHAPTER V

Measures enacted in Colombia

In any historical account of the coca habit it has to be remembered that, from the Conquest up to the present day, rulers, writers, priests and chroniclers in every age have given warning of the danger of the habit. This explains why measures were adopted which, although not sufficient to eradicate the vice completely, at least led to an awareness—if only a faint one—on the part of the authorities of the coca habit and its dangers.

It must be confessed that, in Colombia at least, the uninspiring results of the measures to prevent the cultivation of coca and coca-chewing are exclusively due to the reluctance with which the civil authorities have enforced them. This, in my opinion, is one of the main reasons of the failure of many public health campaigns almost before they are begun; the sole result is a deep disillusionment for the health officials, who, for their part, had attached great importance to the work.

It is equally true that some international bodies whose duty it is to study, solve or keep a watch upon any social problems affecting the peoples of America, should be less passive in their approach to governments. This applies especially to the Commission on Narcotic Drugs of the United Nations, which surely cannot consider it logical that in countries where coca is cultivated and chewed, doctors should have to complete many formalities to prescribe some compound of it, whereas the plant is cultivated freely and the leaf sold publicly in the streets and squares under the indifferent eyes of the authorities.

I feel it is time that organizations such as the International Labour Office, the Commission on Narcotic Drugs, the World Health Organization and even the Pan-American Sanitary Bureau should take joint action to urge governments to comply with the international conventions relating to narcotic drugs and to the suppression of drug addiction. In my opinion, the remedies or measures proposed in Peru and Bolivia, recently visited by United Nations missions, will achieve nothing, because to wait, as they advise, until education and higher economic standards bring about the change in people who have habitually chewed coca for centuries, is as uncertain and slow a process as to expect alcoholism to disappear or diminish in this country so long as the State, as both manufacturer and seller, retains its permanent interest in alcohol.

Action is needed on the part of these bodies to prevent indigenous groups from being destroyed by an age-long vice and human labour from taking the form of veritable slavery; in addition, other bodies, like the Inter-American Indian Institute, should visit all the countries where the Indian is the victim of vices perpetuated solely and deliberately for the purpose of mak-

ing him work more for lower wages. If there were joint action and a real understanding of these problems by all these bodies, the human rights recently affirmed in the United Nations instruments might become something more than a Utopian dream or a thorough deformation of those principles which are broken by the very people who proclaimed them.

Colombian legislation governing cultivation and consumption of coca dates back for barely fifteen years, which shows that this very important problem did not begin to preoccupy the health authorities until 1937.

In that year the National Department of Health, a body which disappeared with the establishment of the Ministry of Labour, Health and Social Welfare in 1938, by Act 95 of 1936, promulgated in 1937, had passed a resolution regulating the traffic in narcotic drugs, but not mentioning the cultivation of and trade in the coca leaf.

In the following year (1938) this resolution was supplemented by Resolution No. 25 of 11 February which provided:

"*Whereas* the Republic is pledged, under international conventions, to supervise the trade in coca leaf

"*Now therefore* the Directorate of the National Health Department in the exercise of its statutory powers, hereby resolves:

"*Article 1.* As from the entry into force of this resolution coca leaf may not be sold except in drug dispensaries and pharmacies, authorized in accordance with the provisions of article 7 of Resolution No. 313 of 1937 issued by this Directorate.

"*Article 2.* Such establishments may not offer coca leaf for sale except on receipt of a medical prescription fulfilling the requirements of article 2 of the annexed Resolution.

"*Article 3.* If any person contravenes the provisions of this Resolution, he shall be liable to a fine of ten (10) to fifty (50) pesos, to be levied by the authorities referred to in article 10 of Resolution 313 of 1937.

"*Article 4.* The present Resolution shall come into effect as from the date of its publication in the *Diario Oficial.*"

Three years later, under the Ministry of Labour, Health and Social Welfare, the above two regulations were supplemented by Resolution No. 578 of September 1941 which stated:

"*Article 1.* As from the date of the entry into force of the present Resolution, all Mayors and Magistrates (*Corregidores*) shall be required to take a census of the plantations of coca (*Erythroxylon coca* and varieties thereof) existing in their respective municipalities and districts.

"This census shall record the number of plants, the area of the plantations, the names of the owners and the annual yield and shall state whether those cultivating the plant sell the leaves thereof.

"*Article 2.* A period of four months is allowed for carrying out the census, the results of which shall, immediately after completion thereof, be transmitted to this Ministry.

"*Article 3.* On the expiration of the above-mentioned period, the sale of coca leaves by wholesale shall be prohibited unless it has been previously authorized by the competent Municipal Health Inspector or, in areas where there is no such official, by the Mayor or Magistrate. Any official who grants such authorizations shall each month transmit a detailed list of the authorizations granted.

"*Article 4.* As from the expiration of a period of thirty days after the publication of the present Resolution no new plantations of *Erythroxylon coca* or varieties thereof may be established in the country. If any are established, they shall be destroyed and the owners thereof shall be punished by fines of not less than 10 pesos and not more than 50 pesos, which shall be imposed by the authorities mentioned in the preceding article.

"*Article 5.* Any plantation existing in national or communal lands shall be destroyed by the competent authorities, who shall duly draw up a report thereon and shall transmit a copy thereof to this Ministry.

"*Article 6.* The sale of coca leaves by retail shall continue to be governed by the provisions of Resolution No. 95 of 1938 of the National Health Department.

"*Article 7.* The present resolution shall come into force immediately on its publication in the *Diario Oficial.*"

When the Ministry of Health was established on 7 January 1947, one of the first measures which I, as Minister of Health, enacted to eradicate coca-chewing was Decree No. 896 of 11 March 1947 (reproduced below) which, as will be noted, refers to the conventions to which Colombia was a party and by which the country was therefore committed to adopt measures such as those contained in the decree in question:

"*Whereas* in accordance with the Conventions signed in Geneva in 1925 and 1931 the Republic is pledged to supervise the production, manufacture, distribution and sale of narcotic drugs; and

"*Whereas* article 1 of Law No. 45 of 1946 prohibits the cultivation and preservation of plants from which the said substances may be extracted; and

"*Whereas* in accordance with article 27, section 1, of Decree No. 2127 of 1945, employers are forbidden to pay wages in kind, vouchers, tokens or by any other means replacing the legal currency of the country,

"*It is decreed that:*

"*Article 1.* The payment of wages or of any kind of emoluments wholly or partly in alcoholic beverages or in coca leaf is prohibited, and agreements or contracts of employment containing any such stipulations shall be null and void.

"*Article 2.* All persons contravening this regulation shall be punished by fines ranging from one hundred (100.00) to five hundred (500.00) pesos, or by imprisonment in lieu of such part thereof as may be provided for by law, such penalties to be imposed by labour inspectors, justices of the peace and other health or police authorities.

"Paragraph. In cases of repetition of the offence, the penalties shall be those prescribed in article 270 of the Penal Code.

"*Article 3.* In accordance with the provisions of article 1 of Law No. 45 of 1946, the cultivation of coca trees (*Erythroxylon coca*) and varieties thereof and of *cannabis sativa* (marihuana) and the distribution and sale of the leaves of these plants, are prohibited in the territory of the Republic.

"*Article 4.* Justices of the peace, *corregidores* and other health and police authorities shall destroy plantations of such trees and confiscate leaves found in the market, other than coca leaves belonging to duly authorized pharmacies, provided that those establishments duly declare them within a period of forty days from the entry into force of this Decree.

"*Article 5.* Any person on whom morphine, cocaine, heroin or any other narcotic drug is found and who has no legal permission to possess them, shall be considered as an illicit trafficker and shall be liable to the penalties prescribed by article 1 of Law No. 45 of 1946.

"*Article 6.* Justices of the peace, *corregidores* and other health or police authorities failing, in any such case, to lay any information before the criminal courts against persons violating this regulation, shall be fined from fifty (50.00) to two hundred (200.00) pesos by their respective superiors, for the first offence, and by removal from office on a second offence.

"For communication and publication
"Done at Bogotá, 11 March 1947
"Mariano Ospina Pérez
"Blas Herrera Anzoategui,
Minister of Labour
"Jorge Bejarano
Minister of Health"

As soon as the above decree had been promulgated, undertakings and individuals interested in the cultivation of and trade in coca promptly organized a virtual conspiracy in the form of a series of complaints and protests, which were more influential than the many expressions of appreciation received by the Government from the Indians.

Other problems, such as the serious strike then affecting the country's largest petroleum-producing area, compelled the Government to enact Decree No. 1472 of April 1947, postponing for one year the order contained in Decree No. 896 to destroy the coca plantations, a postponement which in my opinion was fatal to the campaign. For whenever a radical health measure is subjected to the severe strain of postponement, its complete failure is a foregone conclusion.

That was, in fact, what happened in the case of Decree No. 1472, the text of which read as follows:

"The President of the Republic of Colombia, in the exercise of his statutory powers,

"*Hereby decrees:*

"*Article 1.* The application of article 4 of Decree No. 896 of 11 March 1947 shall be postponed for one year.

"*Article 2.* The *alcaldes, corregidores* and other health and police authorities shall prepare a census of the coca plantations as directed in Resolution No. 578 of 1941 promulgated by the Ministry of Labour, Health and Social Welfare; the census shall record the number of plants, the area of the plantations, the names of the owners, the approximate value of the plantations and the annual yield in kilogrammes.

"*Article 3.* Upon completion of the census, the responsible authorities shall send the results to the Ministry of Health, through the competent *alcaldes*, not later than 1 December of this year.

"Any official who fails to comply with this requirement shall be liable to a fine of fifty (50) pesos, to be imposed by his superior officer.

"*Article 4.* As from the entry into force of this decree, it shall be unlawful to establish any new plantations of *Erythroxylon coca* or of varieties thereof, in the country. If any are established, they shall be destroyed and the owners thereof shall be liable to fines of fifty (50) to one hundred (100) pesos or to imprisonment in lieu thereof as provided by law. These penalties shall be imposed by *alcaldes*, each in so far as he is competent, and shall be proportionate to the number of trees planted.

"*Article 5.* It is the duty of every citizen to report to the competent authorities any coca plantations owned by him and any new plantations which to his knowledge have been planted since the entry into force of this decree."

Very recent reports from Dr. Gerardo Bonilla Iragorri, Director of Health of the Department of Cauca, indicate that coca-chewing and the trade in and growing of coca have again become very extensive in that Department, one of the few still possessing groups of Indians who have relapsed into the baneful coca habit.

In the Department of Cauca, the main production centre, the area of coca plantation covers rather more than one-third of a district that would have acquired great wealth and prosperity if the land had not been devoted to a crop which saps and undermines the fine qualities of the local population. But if we add the ravages of alcoholism to those of the coca habit, we can imagine how dark a future is reserved for that privileged district, which in addition to its incomparable landscape and excellent soil, also has the good fortune to contain the last vestiges of our indigenous race.

The number of people in Colombia who habitually chew coca can be said to be not more than 100,000. Far from lessening the gravity of the problem, this, in my view, increases it, as it shows our complete inability to check in time an evil or vice which is not very extensive at present but which may grow to unforeseeable proportions. Moreover, if the coca chewing were not confined to rural areas and rural peoples, whose physical and mental health ought to receive more care even than of town dwellers, perhaps our continued indifference to so acute a problem would not be so reprehensible. How serious is the damage caused by the coca habit to the economy of the home and of the department is amply illustrated by the comments of visitors to the areas where the vice is prevalent who compared them with areas adjacent to the Department of Cauca, where there is no coca. The difference between them is impressive; the unaffected areas enjoy better health, which is reflected in the whole aspect of the individual, and in the atmosphere of well-being and better living which surrounds him.

To underestimate the problem of coca-chewing in Colombia because the habit as yet is limited to Indian areas — but already shared to an appreciable extent by white and mixed peoples in areas outside the strictly Andean region — is neither humane nor politic.

This would simply mean that Latin America is still under the spell of the hispanizing policy which prevents us from integrating into our social life indigenous peoples or groups whom we accordingly still treat with irritating disdain and even with inhuman cruelty. While it is true that the policy of extermination and destruction of the indigenous population is no longer in effect, it is no less true that we have left the indigenous population to its traditional vices for even our scanty scientific and sociological researches concerning the indigenous population contain abundant and reproachful evidence to show that we have idly witnessed its total disintegration under the effects of age-old vices.

Nor has the problem of coca-leaf chewing, viewed from that angle, received more than superficial attention from our health authorities, for it is commonly believed that the habit, which, as we have seen, has been indulged in by the indigenous population since time immemorial, is harmless since it has not occurred to us to compare it to cocaine addiction to which it is really equivalent.

It was left to Bolivian and Peruvian physicians, who are thoroughly familiar with the coca habit and its manifestations, to show that the chewing of fifty grammes of coca leaf per day releases a quantity of at least 39 centigrammes of cocaine, a strongly toxic dose, particularly when taken every day for life.

As Professor Emilio Fernández of Bolivia has said: "Whereas cocaine addiction is a vice connected with cabarets and practised by women of ill repute and their associates, the coca habit by contrast occurs among the indigenous population, the rural population and miners."

The comments on the coca habit in Bolivia by Professor Juan Manuel Balcázar who, with Professor Fernández, is the leading research worker investigating this serious Bolivian problem, are most impressive. He says: "The annual production of coca is 3 million kilogrammes, all of which is consumed in Bolivia. This quantity of coca is sufficient to produce 20,000 kilogrammes of cocaine per year which is used to intoxicate the rural population. That intoxication costs the country 400 million bolivianos which represents a loss to the country's economy and which is expended in keeping one-third of the Bolivian population in a state of intellectual abjectness and physical prostration".

Professor Balcázar's analysis is applicable to our problem in Colombia, though in our case, as mentioned before, the situation deserves even greater censure because our problem, being on a smaller scale, ought to have been remedied by drastic action long ago.

CHAPTER VI

Co-ordination of agencies in the campaign against the coca habit

When Decree No. 896 of 1947 was promulgated, I, as Minister of Health, wished the campaign to be co-ordinated with the Ministries of Labour and Agriculture, the Agrarian Fund, the Land Credit Institute and the banking institutions.

The co-ordination was not achieved at that time, but it is essential if success is to be won against all the influences adverse to action which ought to be drastic.

The Ministry of Labour is the agency responsible for posting an adequate number of labour inspectors in the areas where coca is cultivated in order to keep watch and punish those who pay part of their workers' wages in coca leaves. The Ministry of Labour could easily order the inspectors to examine the amount actually received. If there is one duty which the Ministry in question ought to perform at this time, it is to ensure compliance with the legislation relating to labour, public health and industry.

In my opinion, the Ministry of Agriculture is the proper agency to encourage many of the public health campaigns. The replacement of crops, like coca, which contribute nothing to the nation's food, by others which are economically more useful and profitable, is one of the most appropriate functions of that Ministry in Colombia as well as in other countries of Latin America. Rational feeding and the control of many infectious and social diseases and of avitaminosis present problems which cannot be resolved by public health alone, even with vast resources. Perhaps the most important mission of Ministries of Agriculture today is to encourage the production of food, to open up new areas and centres of production, and to introduce technical knowledge in agriculture.

The Agrarian Fund jointly with the Ministry of Agriculture should help in solving the problem by supplying tools and seeds to encourage new crops as substitutes for coca.

The Land Credit Institute, a Colombian agency concerned with improving rural housing, should also participate in this campaign. Unhealthy and wretched living conditions are notorious sources of infections and social diseases and of avitaminosis. The indigenous inhabitants in Latin America continue to live in the same primitive conditions as their earliest forefathers. All we have done to civilize them was to impose religion on them, but their environment of poverty, ignorance and unwholesome conditions is far inferior to anything that the men who destroyed the indigenous culture can possibly have found.

Housing also materially influences human behaviour. The wretched hovel which is the Indian's shelter can fill the family with nothing but disgust and hatred; it cannot ennoble the personality, or breed anything but vice and crime.

The indigenous inhabitants have not as yet been touched by the benefits of hygiene in the form of wholesome dwellings. If standards based on the technique and spirit of prophylaxis had been adopted in the construction of rural housing in Colombia, the last fifteen years would have witnessed a transformation in rural housing in keeping with the objective of controlling endemic diseases and counteracting social maladjustment, which are the accompanying features of insanitary housing.

Finally, it is my opinion that the country's banking institutions should co-operate in the solution of many social and health problems by offering financial facilities on special terms to persons who are to replace coca by other crops more useful to the community. A system whereby these loans would be insured by the Agrarian Fund itself might be one of the ways of enlisting the support of some growers and of impressing them with the noble function which tilling the soil ought to be.

Conclusions

1. It is an accepted and scientifically proven fact that coca-leaf chewing as practised by the indigenous inhabitants of Bolivia, Colombia, Ecuador and Peru is a form of drug addiction with effects analogous to those produced by cocaine, which is the alkaloid of coca.

2. At the invitation of the Governments of Peru and Bolivia, the United Nations Economic and Social Council sent a Commission of Enquiry to these countries in 1949 to determine the effects of coca-leaf chewing and to consider the possibility of limiting coca production and distribution.

3. After careful study in the coca-chewing areas of both countries and after exchanging views with the scientists in Bolivia and Peru who had thoroughly studied the effects of the coca habit, that Commission concluded by recognizing the harmful nature of the habit of coca-leaf chewing which is detrimental to the individual and to society.

4. In the light of science and experience, none of the arguments to justify the harmful coca habit can now be accepted. Accordingly, the consumption of coca is not necessary to support life at great altitudes because life at these altitudes depends only on general living conditions, the diet and the individual's ability to obtain sustenance.

5. The pseudo-scientific thesis that the inhabitant of the Andes is a climato-physiological species of the human race who needs coca to adjust himself to the environment in which it is his lot to live, is an artful fallacy refuted by such incontrovertible facts as that other races, entirely alien to the environment, have not needed coca in order to adjust themselves perfectly to the environment of the Andes. How is it (we might ask) that individuals accustomed to coca can perform their military service in Bolivia and Peru and do not suffer any ill effects owing to maladjustment to the environment when they are abruptly deprived of the drug which is believed to be the adjusting agent?

6. It has been demonstrated in countries with long experience in observing the coca habit that coca is not necessary and rather highly detrimental to the performance of the worker.

7. The coca habit in Colombia is such that the Government is under a duty to resume, without faltering, the campaign contemplated in Decrees Nos. 896 and 1432 of the Ministry of Public Health.

8. The fact that coca cultivation is fortunately still confined to a few areas makes it even more imperative to take steps without delay to prevent the evil from spreading and assuming greater proportions.

9. Though Colombia is a party to international conventions to suppress drug addiction, it is failing to comply with treaties requiring it to combat drug addiction within its own borders. It is illogical that the cultivation of Indian hemp or marihuana, for example,

should be regarded as unlawful, while the cultivation of coca, which is equally harmful and dangerous, is tolerated.

10. The campaign against the cultivation of coca should be followed by effective assistance from the agencies mentioned in chapter VII of this study.

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Another drug is placed under international control

The international conventions on narcotics provide means whereby control can be applied to substances that were unknown or not in use at the time those instruments were concluded. Thus, article 10 of the 19 February 1925 Convention makes it possible to place under control any narcotic drug to which the Convention does not apply, if the World Health Organization establishes that it is liable to be abused in the same way as the drugs covered by the Convention and to produce similar ill effects.

Article 11 of the 13 July 1931 Convention for limiting the manufacture and regulating the distribution of narcotic drugs, foresees a special procedure for submitting to the control any product obtained from any of the phenanthrene alkaloids of opium or from the ecgonine alkaloids of the coca leaf not in use at the time the Convention was signed for medical or scientific purposes.

But, whereas the control foreseen by the 1925 Convention has only a restricted scope and is subject besides to the acceptance, by the contracting Parties, of the World Health Organization recommendation on the drug concerned, the control established by the 1931 Convention is more strict and has to be applied automatically by all contracting Parties on reception of the notification from the Secretary-General of the United Nations.

Those synthetic narcotics which are not covered by the 1931 Convention can however be placed under the control provided by that instrument, through the application of the procedure set up by the Paris Protocol of 19 November 1948.

The Parties to that Protocol shall, upon receiving the communication from the Secretary-General notifying the decision of the World Health Organization, apply to the new drug the appropriate régime foreseen by the 1931 Convention. However, since the Protocol has so far been ratified by only thirty-seven States, application of that instrument is thereby limited to that number of States, whereas the control applied to a drug by virtue of the 1931 Convention, which has been ratified by more than sixty States, has consequently a much more general scope.

Recently, the provisions of the 1931 Convention were applied to a product manufactured in France and known by the name of "β-4-morpholinylethylmorphine". The procedure was started in September 1949 when the French Government addressed a notification to the Secretary-General asking that article 11 of the 1931 Convention be applied to the substance mentioned above, and in particular that it be considered as belonging to Group II.

According to the provisions of this article, any government authorizing trade in or manufacture for trade of any product obtained from any of the phenanthrene alkaloids of opium or of the ecgonine alkaloids of the coca leaf, not in use for medical or scientific purposes at the time the Convention was concluded, shall immediately notify the Secretary-General of the United Nations, who shall advise the other High Contracting Parties to the Convention and the World Health Organization. The latter, acting on the advice of a Committee of Experts appointed by the World Health Organization, will thereupon decide whether the product in question is capable of producing addiction or is convertible into such a drug. In the first case, that product is considered as one of the drugs mentioned in the Convention under Group I. In the second case, the question is submitted to a body of three experts who determine whether the product falls under sub-group (*b*) of Group I or under Group II. Two of those experts shall be appointed by the Government concerned and by the Commission on Narcotic Drugs respectively, and the third expert by the other two. It must be explained that the Convention sets up a different control for the drugs in Group I and for those in Group II, this control being stricter for the drugs under Group I. Until a decision is arrived at concerning the definitive classification of the product under consideration, the Government concerned, unless it determines that this product is not capable of producing addiction or of conversion into a product capable of producing addiction, shall be bound to limit its fabrication to quantities not exceeding the total of the domestic requirements of the country for medical or scientific needs, and the quantity required for export orders; it shall also apply to this product the provisions of the 1931 Convention. The Conference which adopted the 1931 Convention considered that in this instance it is the régime provided for the drugs under Group I that must be applied.

At the same time as the notification addressed to the Secretary-General, the Ministry of Public Health

and Population of the French Republic transmitted a Note in which it was indicated that the product under consideration is marketed by the Dausse Laboratories in Paris, as a proprietary drug under the name of "hibernyl" which is offered:

1. As a syrup containing 0 gr. 10 phenylacetate of morpholinylethylmorphine per 100 gr. of syrup

2. In tablets containing 0 gr. 015 of morpholinylethylmorphine phenylacetate per tablet.

This note ended up with the remark that "in view of its low toxicity (three times less than that of codeine), its effectiveness (always equal to and frequently greater than that of codeine), and its lack of untoward side-effects, morpholinylethylmorphine constitutes a noteworthy therapeutic advance on codeine". The Dausse Laboratories received the authorization, pursuant to international conventions and to French regulations, to manufacture and market this product under licence.

The Secretary-General transmitted the notification from the French Government to the other governments Parties to the 1931 Convention as well as to the World Health Organization. The latter entrusted its Committee of Experts on Drugs Liable to Produce Addiction with the task of looking into the French request. This Committee, on the basis of the available documentation, was of opinion that there was insufficient evidence to permit a decision on the addiction-producing properties of morpholinylethylmorphine although it must probably be convertible to morphine and that, in any case, as an ether-oxyde of morphine, that substance was by definition in sub-group (*b*) of Group I of the 1931 Convention.

When the Commission on Narcotic Drugs, at its fifth session in December 1950, considered the report of the Expert Committee (of WHO) on its second session, and particularly the item dealing with morpholinylethylmorphine, the French representative requested that the committee of three experts, provided for in paragraph 4 of article 11 of the Convention should be set up. This proposal gave rise to an exchange of views and the opinion was expressed then that the fact of classifying automatically morpholinylethylmorphine under sub-group (*b*) might give rise to objections since codeine, another ether of morphine, was placed under Group II. The Commission finally decided to request the Secretary-General to invite the World Health Organization to re-examine the question in the light of fresh information which the French Government might make available.

The World Health Organization studied the supplementary documentation put at its disposal by France and transmitted to the Secretary-General, in February 1952, the text of the new findings formulated by its Committee of Experts. In the terms of this finding, "β-4-morpholinylethylmorphine" is not more liable than codeine to produce addiction and is therefore not assimilable to the drugs mentioned in sub-group (*a*) of Group I; on the other hand it is less readily convertible than codeine to an addiction-producing drug and is, in consequence, assimilable to the drugs under Group II.

This finding was brought to the knowledge of governments by a Note from the Secretary-General of the United Nations which pointed out that the World Health Organization had, in fact, decided that, without being a drug liable to produce addiction, morpholinylethylmorphine could be transformed in such a drug. The Secretary-General, therefore, drew attention to provisions of paragraph 4 of article 11 which provide for the constitution of a body of three experts.

The Commission on Narcotic Drugs itself, at its seventh session in April and May 1952, took note of the findings of the World Health Organization in the matter and in view of the substance of these findings decided to appoint one of the members of the body of three experts, i.e., Mr. A. Kruysse, representative of the Netherlands. At the same time, the French Government advised the Secretary-General that it had appointed Mr. Charles Vaille, representative of France on the Commission on Narcotic Drugs to serve on this three experts' committee. Messrs. Kruysse and Vaille in their turn designated as third expert Mr. P. O. Wolff, Chief of the Section of Drugs Liable to Produce Addiction (World Health Organization), who was representing that Organization at the seventh session of the Commission on Narcotic Drugs. The three experts met during the session of the Commission and, after having elected Mr. Wolff President of the committee, they decided that "β-4-morpholinylethylmorphine" should be placed under the régime of control which applies to drugs included in Group II. They transmitted this decision to the Secretary-General of the United Nations who communicated it to the governments in accordance with the provisions of article 11, paragraph 5.

It should be mentioned that it is the first time since the Convention of 1931 came into force that the procedure provided for by article 11, paragraph 4, has been applied.

The swiftness with which the Commission on Narcotic Drugs, as well as the three experts designated to sit on the committee, acted made it possible to close without delay the procedure followed to give effect to the initial request of the French Government. The length of this procedure at its early stage was due to the necessity of taking into account the various technical and legal aspects of the problem under consideration.

CORRECTIONS

"Preparations exempted from the control measures of the Narcotic Conventions" *Bulletin on Narcotics,* Vol. III, No. 4, October 1951.

The following preparations should be deleted from the list of those exempted from the control measures:

36. Sterilized solutions of morphine and atropine (page 6).

51. Sterilized solutions of eucodal and atropine (page 8).

The exemptions given these preparations by the Health Committee of the League of Nations were later rescinded by the same Committee (C.426.M.218.1935. III). This decision was notified to governments in circular letter C.L.162.1936.XI, but the letter made no mention of the necessity of correcting the "Recapitulatory List" (C.114.M.54.1932.III).

In formula 22, *Suppositoria Plumbi composita,* the amount of lead acetate, in powder, should be 2.4 grammes, not 12.4 grammes (page 5).

* * *

In the same issue, in the paper "Note on the total synthesis of morphine", p. 34-35, formula V should read:

(1) instead of β-thebainone, β-dihydrothebainone;

(2) instead of the double bond on the right-hand ring, there should be a single bond.

The value of bioassays in detecting narcotics

By James C. Munch,[1] Aaron B. Sloane[2] and Albert R. Latven[2]

This article relates how a biological method was evolved and developed, by means of injections to mice, whereby "doping" of race-horses could be detected in a matter of minutes

Narcotics have a recognized and valuable place in drug practice; unfortunately, there has been a great tendency for diversion into improper channels. The chemical procedures developed throughout the world have permitted official standards in the various national pharmacopoeias; standards have been set for opium preparations and their alkaloids, for example, based upon these chemical procedures.

Pharmacological investigations have pointed out that the various alkaloids in opium influence the pharmacodynamic responses of the individual alkaloids, both qualitatively and quantitatively. Certain alkaloids in opium tend to increase the effect of morphine, additively or synergistically; other alkaloids in opium tend to decrease the morphine effect in men or other animals. For this reason, the chemical assurance that a number of lots of opium all contain 10 per cent of morphine is not necessarily a proof that the different lots of opium will have identical clinical effects. With this in mind, investigations have been conducted in various laboratories for the purpose of developing pharmacological habits of evaluating opium. Presumably, similar findings will be encountered in a thorough study of other narcotics.

Some years ago the illegal diversion of heroin and of morphine from legitimate drug channels for the purpose of "stimulating" race-horses was learned as the result of field inspections by agents of the Federal Bureau of Narcotics of the United States Treasury Department. Under the authority of the Harrison Anti-Narcotic Act, investigations were started to determine the extent of such illegal diversion. A series of conferences was called by the Honorable Harry J. Anslinger, United States Commissioner of Narcotics. These were attended by chemists, pharamacologists, and veterinarians, who discussed the broad bases of investigations and arranged for a co-ordinated research programme for the purpose of detecting the "doping" of race-horses (the illegal administration of drugs, such as morphine or heroin).

From these conferences, and investigations conducted by the members of this group under the general direction of the United States Government, various state and local agencies, state racing commissions and owners of race-horses, substantial research was conducted which led to a series of procedures for the detecting of "doping". Samples of saliva, of urine, of sweat and of blood were obtained from horses before and after the administration of various products. Tests were made on these samples by laboratory workers. The samples were usually submitted in code so that the identity of the animal and any treatment it might have received were unknown to the testing groups. From this emerged a definite chemical technique for extraction and identification of various products. For various reasons it was not feasible to conduct investigations routinely on sweat or on blood, so these methods were directed specifically to analyses of the saliva and of the urine. The methods of determining various poisons in tissues, as set forth in standard toxicologies, were modified to meet requirements for this specific study. Various new solvents were developed for shake-out processes. The limited quantities of saliva or urine which were available, and the peculiar nature of the physiological constituents of these fluids, required special modifications in chemical technique. From these studies, a definite method of procedure evolved.

Since a period of forty-eight hours is often required for complete examination, and since the chemical studies of the end extraction processes could only be used with materials of certain chemical stability, it was thought that certain products, such as hormones, would not be detected by these methods. Definite metabolic changes occur during the passage of these materials through the body of the race-horse or other animal, i.e., the substances excreted in the saliva and the urine may be chemically different from the products which were administered originally. Because of the complicated metabolic pathways for various products in the animal or human system, it becomes very difficult to determine

[1] Medical Director, Strong, Cobb & Co. Inc., Cleveland, Ohio, U.S.A.

[2] Munch Research Laboratories, Inc., 306 S. 69 St., Upper Darby, Pa., U.S.A.

strange or unusual products, or even the usual degradation products of many materials. With this in mind, the pharmacologists in the original conferences thought that it would be worth while to make detailed studies of the pharmacological methods for detection of drugs which might be employed for the purpose of "doping" horses. While these investigations are still under way in our laboratories, it appears helpful to summarize results to date for possible co-operation with interested pharmacologists throughout the world.

Our investigations have been conducted upon many species of animals but we finally decided that mice are the most satisfactory. The quantities required to produce effects on cats or dogs are much greater than those required to produce effects on mice. Standard strains of mice are readily available in large numbers (subject at times to demands of governments interested in the production of drugs and in their testing).

Furthermore, it was found that mice showed rather uniform pattern of behaviour. Observations of a large number of animals under identical conditions permitted the determination of their activity, or any characteristics of action which might be typical of the groups of mice under investigation. While it is possible to give doses of drugs by mouth, intravenously or by other routes, it was found that intraperitoneal administration was feasible, rapid and satisfactory for this purpose. Studies on horses which had not received any medication within a period of twenty-four hours indicated that 2.0 cc. of saliva or of 1.0 cc. of urine per mouse did not produce any toxicologic effects within 10-15 minutes. Occasional mice showed some sedation as a result of the administration of a quantity of fluid corresponding to more than one-tenth of the body weight, but these effects were readily distinguishable from those following the administration of pharmacologically active drugs. Studies on saliva or urine from several thousand unmedicated horses have failed to reveal any symptoms in mice which could be mistaken for those following administration of drugs.

When drugs were administered to race-horses, samples of saliva and of urine collected within a period of several hours were capable of producing effects in mice. After administering large doses of drugs, positive reactions were observed following intraperitoneal injection into mice of quantities as small as 0.1 cc. per mouse. As a matter of uniformity, it was deemed advisable to develop a method by which one or more mice would receive intraperitoneal injections of 0.5 cc. per mouse while the others would receive 1 cc. each. Depending on the result of these tests, it was always possible to give larger or smaller doses as desired. A further advantage in the use of mice is that the volume of fluid required is small. This is desirable since the quantities of saliva or urine submitted for test are often limited.

The technique to be followed is simple. Groups of white mice of a standard strain from a recognized dealer are offered a standard diet and kept under observation for a period of several days. Animals in good condition are then selected at random from the colony. Either males or females may be used although we have felt that females were somewhat more susceptible. Mice from different sources will differ significantly in their sensitivity. For this reason we have preferred to use CFCW or CF-1 mice furnished by Carworth Farms, Rockland City, New York. When conducting tests at the race-tracks, it is necessary that prior arrangements be made to permit drop shipments of mice at weekly intervals. The diet of the mice is that recommended by the Carworth Farms, although any standard food for animals may be employed.

Mice are removed individually from a colony and intraperitoneal injections of 0.25 cc., of 0.5 cc. and 1.0 cc. given. After injection, the animals receiving the same sample are placed in the same cage and observed continuously for a period of five to ten minutes. Other doses may be used, if desired. Also, observation periods may be extended to two hours if warranted.

In our experience on several thousand samples of saliva and urine obtained from horses which had not been given drugs within twenty-four hours, no changes in behaviour, appearance, or attitude developed in the mice. If the volume administered is 2 cc. or more per mouse, some depression and sluggish gait may develop as a result of the volume effect. The same effects may be produced by administration of heroic volumes of 0.9 per cent sodium chloride solution or other inert solutions. If these animals are observed for several hours, it is rare to note any symptoms which simulate those produced by drugs used for "doping" horses. Since the samples are not sterile or sterilized, intraperitoneal injection usually leads to infections and death after twelve to twenty-four hours, but this is a bacteriological rather than a pharmacodynamic response.

When effective drugs have been deliberately added to samples of saliva or urine, or when these fluids were collected from horses which had previously received effective drugs within a period of twenty-four hours or less, changes developed in the test mice. These alterations in behaviour, appearance or condition developed within 5 to 10 minutes and were obvious alterations from the pre-injection state.

The symptoms and signs which develop depend on the nature of the product administered. Following injection of the barbiturates, or sedatives in general, sluggishness, decrease in voluntary travel, and a tendency to sleep are noted. With increasing quantities of administered drug, symptoms develop more rapidly and to greater intensities. On the other hand, strychnine or caffeine tend to produce increased locomotion, increased respiration, and muscular tremors. These symptoms may progress to definite prostration, coma, and death, if the quantity of drug administered is sufficient.

In learning the technique, known samples of materials may be dissolved in saliva, urine, or distilled water. By injecting a series of animals with various doses, it is possible to determine the threshold dose, i.e., that quantity of material which is capable of producing discernible or detectable alterations in mice under the conditions prevailing in the testing laboratory. Passage of a drug through the horse produces metabolites which may cause symptoms differing from those produced by the original drug.

It is recognized that some animals are more sensitive than others. Certain workers are able to detect alterations more readily. For this reason, it is important that each laboratory should standardize itself, i.e., administer a known sample of a test product at various dosage levels to substantial numbers of mice and determine the effects produced at the different levels. It is also possible to determine the character, type and extent of departures from normal behaviour that will be produced by differing quantities of a product under individual laboratory working conditions. Based upon our studies, the threshold doses established for a number of products are recorded in table I. While the absolute values may differ under varying conditions of test, our experience has indicated that there is a proportional relationship between these threshold levels. This emphasizes the previous point that every laboratory should determine its own threshold values.

We have also established the finding that many narcotics are altered in the body during the process of absorption, distribution and elimination. For example, heroin is converted to a large extent to morphine in the body as suggested by differences in threshold doses and symptoms produced. After completing a series of studies with known drugs, it is possible to develop criteria by which many of the narcotics used in the "doping" of race-horses may be identified qualitatively. A semi-quantitative estimate may also be made by determining the smallest volume of test solution capable of producing the recognized reaction following the established threshold dose.

Of course, it has been desirable to conduct chemical examinations on those samples of saliva or urine which have proven positive by bioassay, for the purpose of identification of the drug or drugs present. The bioassay is very sensitive and is able to detect threshold quantities which are usually less than those required for definite chemical identification. Furthermore, the biological responses will follow administration of impure materials and their metabolites, as distinguished from definitive chemical methods which require substantially pure test material. If several products are present in the saliva or urine the animals usually show mixed responses, which indicate the nature of the several drugs present. For example, strychnine tends to produce increased respiration and muscle tension. Heroin or morphine tend to produce a characteristic S-curve of the tail of the mouse. If a combination of both products is administered, both types of effects may be observed.

We have extended our investigations to include trials of saliva and urine from animals other than race-horses and find equal satisfaction in the testing process. We have done some work on the saliva and urine of humans and find that the biological method permits identification of "dope addicts", as well as malingerers.

Surviving animals can be re-used after an interval of several days if test solutions have been prepared in distilled water. On the other hand, if solutions of saliva or urine have been administered, in our opinion the animals should not be re-used. While the cost of animals varies, arrangements can usually be made by which the cost is around $0.30 per mouse. Using a total of four mice on a single test, this makes the cost of animals about one dollar. No other expenses are incurred, with the exception of the feed and care of the test animals. Results of tests on a preliminary group may be confirmed on additional mice at a slight increase in cost. The amount of the saliva or urine used is relatively small, and the results of the biological assay will be helpful in orienting chemical tests on the remainder for identification of the suspected drug or drugs. In our experience, we have never had positive chemical tests on saliva or urine samples which were negative by the biological test. The converse is not true; we have had positive biological tests following administration of many materials for which adequate chemical methods were not available.

A further advantage of this biological procedure may be pointed out, namely, that the positive results will be obtained in ten minutes or less if tests are made on saliva samples from a race-horse. This permits pre-race testing of horses almost immediately before they are led to the track. This is an advantage which has not been established for the chemical assay since the process requires several hours, even up to two days for separation and purification of extracts before tests for chemical identification can be conducted. Of course, it is recognized that both biological and chemical tests have their peculiar and distinctive values. Before legal hearings which might lead to disbarment of accused persons are held it may be desirable to have both biological and chemical support for the charge of "doping".

After establishing the method of procedure in our laboratory, we worked with the Maryland State Racing Commission and Mr. Mahoney in the development of a mobile laboratory unit for use at the race-track. This proved an advantage in that it permitted cooperation between the pharmacologist and the chemist at all times; it permitted specific leads from pharmacological behaviour to orient special chemical extraction processes; and it made it unnecessary for the chemist to make examinations on samples that were negative by biological test. This saved time and the chemist could concentrate on the positive samples. It was pos-

sible to get saliva samples from all of the horses entered in every race during the course of a day (which might be as many as 80 or 90 samples), instead of examining only samples from the eight which had won their respective races. The "doping" of horses which finished in the second, third, or fourth places was more frequent than in the winning horses.

Summarizing, a biological method has been developed for the detection of narcotics in the saliva or urine of "doped" race-horses, which has also been valuable in detecting the use of these drugs by humans. It consists of the intraperitoneal injection of 0.25 to 1.0 cc. of test solution to each of a number of white mice and observation of any changes in behaviour which may develop within a period of ten minutes. Saliva or urine samples from several hundred horses which were not given drugs consistently produced negative results. Samples from horses deliberately "doped" (unknown to the bioassayist) were consistently identified by the biological method. Depending on the nature of the product administered, chemical tests may or may not be correct; we have never obtained positive chemical findings on saliva or urine samples which were negative by the mouse test. Following administration of certain products to race horses, we have obtained positive biological responses but negative chemical tests. Using the biological test, it is possible to make pre-race investigations of all the horses entered in races. By using a mobile field laboratory unit, both chemical and pharmacological tests may be made at the race track. These tests have been conducted under the direction of a number of the state racing commissions in the United States. Positive biological tests should be confirmed by chemical examinations before legal steps are instituted. The possibilities of the biological method are being investigated further.

The authors wish to express their appreciation to the Honorable Harry J. Anslinger, United States Commissioner of Narcotics, and to the various officials of the Racing Commissions of the States of Maryland and Washington, particularly Mr. George R. Mahoney, former chairman of the Maryland State Racing Commission, for assistance in arranging for these studies. They also wish to acknowledge the support and cooperation of the various members of the National Horsemen's Benevolent and Protective Association.

TABLE

Thresholds for detection by mice; intraperitoneal injection

Drug	*Micrograms/ 20 gram mouse*
Amphetamine	80
Caffeine	600
Cocaine HCl	400
Codeine	60
Coramine	100
Pethidine	400
Desoxyephedrine	40
Dihydromorphinone	12
Ephedrine	200
Heroin	1
Morphine	60–80
Picrotoxin	40
Strychnine	1(?)

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The synthesis of papaverine

By Dov Elad and David Ginsburg

The Weizmann Institute of Science, Rehovoth, Israel

Although papaverine is not under international narcotics control it is an opium alkaloid and so within the interest of readers of the Bulletin. Medical use has created a demand in excess of the supply obtained from opium. This article reviews the methods of synthesizing this alkaloid

Papaverine (1-(3,4-dimethoxybenzyl)-6,7-dimethoxyisoquinoline) is a member of the benzylisoquinoline sub-group of the opium alkaloids and is present in most varieties of opium to the extent of 0.5 to 1 per cent. Since the alkaloid is one of nature's useful antispasmodics, it soon found its way into the physician's arsenal, and serves in cases when it is necessary to cause relaxation of smooth muscle. Papaverine, in the form of its hydrochloride, is administered intravenously in treating pulmonary arterial embolism and orally or by injection in treating renal or biliary colic. It is not effective in abolishing neurally excited spasms and has undesirable side-effects, such as causing prolonged fall in arterial blood pressure, when the intestinal tract is relaxed. This is due to lack of selectivity in relaxing smooth muscle. Despite such undesirable side-effects, nature does not produce enough papaverine to meet the demands of medical practice, and many syntheses have been devised for preparation of this alkaloid. It is the purpose of this article to review the published methods for the production of synthetic papaverine.

A short account of the researches leading up to the assignment of the structure of papaverine, would, perhaps, be in order. Papaverine was first isolated by G. Merck,[1] in 1848, who assigned to it the correct empirical formula $C_{20}H_{21}O_4N$. The structure of the alkaloid was determined mainly by Goldschmiedt and his co-workers.[2] Some confusion existed in the early work through the misconception that a quinoline nucleus was present in papaverine. It was later shown,[8] that an *iso*quinoline nucleus is present.* The most important data regarding the structure were obtained by means of oxidative degradation.

Papaverine, upon oxidation with permanganate under different conditions of pH, yields a variety of degradation products. Among these are 6,7-dimethoxyisoquinoline-1-carboxylic acid (I), 6,7-dimethoxyisoquinoline (II), metahemipinic acid (III), and cinchomeronic acid (IV).

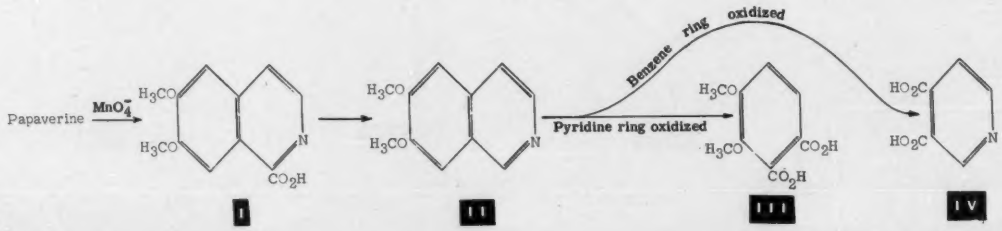
The formation of these products is consistent with the following formulation:

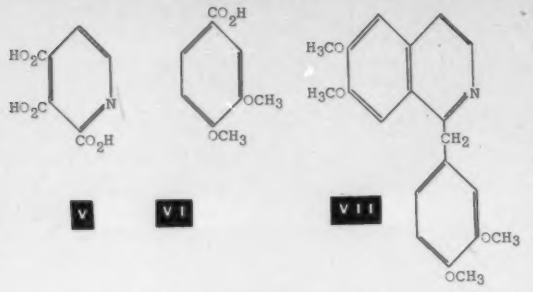
The point of attachment of the veratryl residue was demonstrated by oxidation with hot permanganate. Under these conditions, pyridine-2, 3, 4-tricarboxylic acid (V) was isolated. The veratryl residue appeared in the oxidation mixture in the form of veratric acid (VI). Structure VII was therefore assigned to papaverine.

Since this structure is relatively simple, it was soon proved by synthesis. A number of improvements have been made since the original synthesis, which considerably simplify the preparation of papaverine. Synthetic papaverine has out-distanced the naturally occurring alkaloid in volume of production.**

* See VII.

** The reasoning applied in correcting the early misconception is of great interest but is beyond the scope of this article. For a discussion, see reference 4. References will be found at the end of this article.





V VI VII

The first synthesis of papaverine was accomplished by Pictet and Gams.[5] The synthetic sequence is shown in chart I.

The two intermediates in this synthesis are 3,4-dimethoxy-ω-amino-acetophenone (XI; chart I, (*a*)) and homoveratroyl chloride (XVI; chart I, (*b*)).

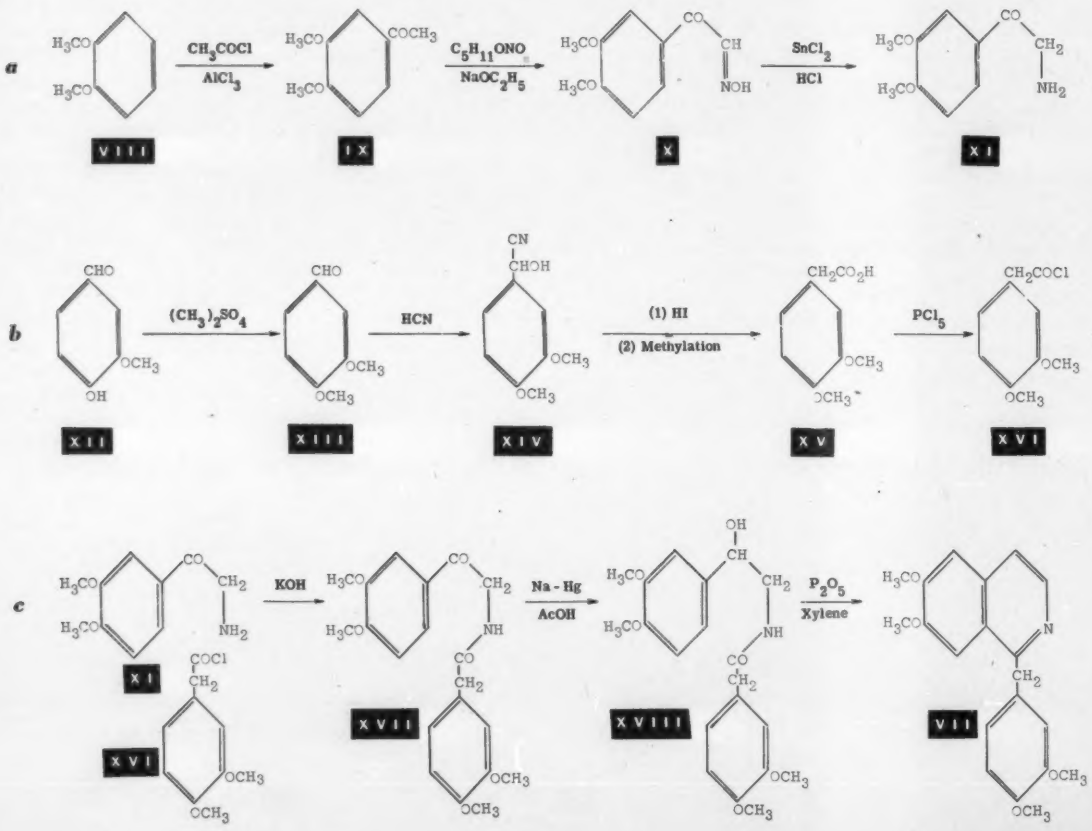
3,4–dimethoxy-acetophenone (IX) was obtained through a Friedel-Crafts reaction of veratrole (VIII) with acetyl chloride. This ketone was converted through the oximino-ketone X to the corresponding ω-amino-acetophenone XI by reduction with stannous chloride.

Veratric aldehyde (XIII) was obtained by methylation of vanillin (XII). The cyanohydrin XIV was prepared and upon treatment with hydriodic acid, several transformations took place: demethylation of the phenolic ether groups, saponification of the nitrile group and reduction of the secondary hydroxyl group. Remethylation of the product gave homoveratric acid (XV) which was converted to its acid chloride (XVI) by means of phosphorus pentachloride.

Condensation of the hydrochloride of 3,4-dimethoxy-ω-amino-acetophenone (XI) with homoveratroyl chloride (XVI) yielded the β–keto–amide XVII. Reduction with sodium amalgam gave the corresponding β–hydroxy–amide XVIII. Dehydration of XVIII with phosphorus pentoxide at the reflux temperature of xylene yielded papaverine (VII).

Pictet and Finkelstein[6] improved the synthesis by substituting β–(3,4–dimethoxyphenyl)–ethyl amine (XIX) for the above ω–amino–acetophenone. Con-

Chart I.



densation of this amine with homoveratroyl chloride yielded the amide XX. Cyclization of the amide by the Bischler-Napieralski procedure (phosphorus oxychloride), yielded 3,4–dihydropapaverine (XXI). It remained to Späth and Burger[7] to accomplish the dehydrogenation of this substance, by treatment with palladized-asbestos at 200° in the presence of air. The latter workers showed also that 1, 2, 3, 4–tetrahydropapaverine (XXXIII) could be dehydrogenated to papaverine by means of the same catalyst. The reactions discussed are summarized in chart II.

Two groups, headed by Rosenmund and Mannich, respectively, employed 3,4–dimethoxy–ω–nitro–styrene (XXII) as an intermediate in the synthesis of papaverine.[8, 9] This approach makes use of the observation that alcohols can be added to the double bond of ω–nitro–styrenes and is summarized in chart III.

The ω–nitro–styrene XXII is obtained by alkaline condensation of veratric aldehyde (XIII) with nitromethane. The methyl ether XXIII is obtained by the addition of the elements of methanol to the double bond of XXII. Reduction either with zinc-copper alloy in the presence of formic acid or with sodium amalgam in the presence of acetic acid, gives the methyl ether of the corresponding amine (XXIV). Treatment of the latter with homoveratroyl chloride yields the methyl ether XXV of the β–hydroxy–amide (XVIII) which is an intermediate in the original Pictet-Gams synthesis. In analogy to that synthesis (in which two moles of water were removed in the final cyclization

Chart II.

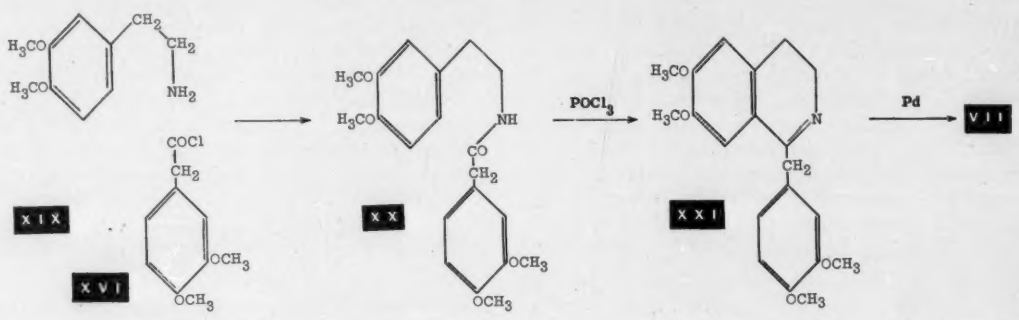
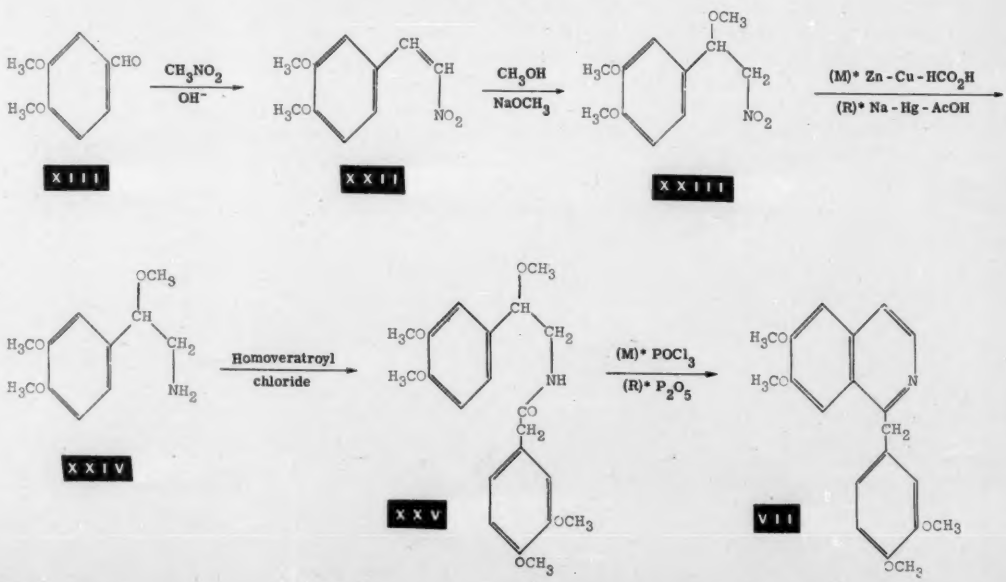
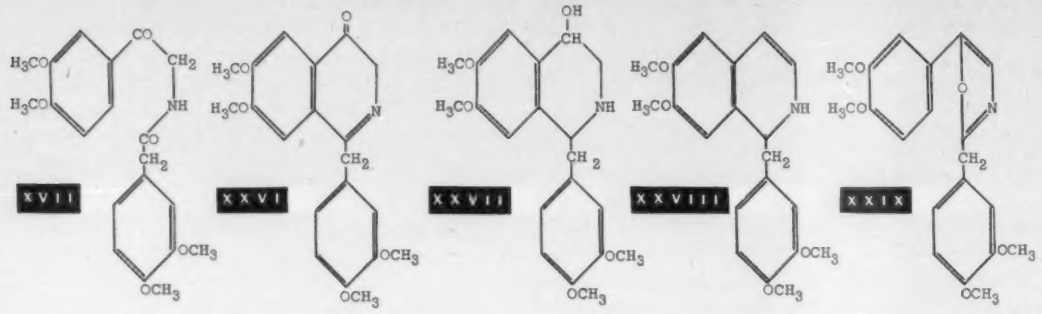


Chart III.





step), one mole water and one mole methanol are removed by a cyclization agent, and papaverine is formed.

Buck[10] dehydrated the β-keto-amide which had previously been obtained as an intermediate in the Pictet-Gams synthesis, by means of phosphorus oxychloride, and formulated the product as XXVI. This was reduced with a palladium-platinum catalyst to a product formulated as XXVII and the latter was dehydrated by means of phosphorus pentachloride in chloroform to a crystalline substance formulated as 1,2–dihydropapaverine (XXVIII). That this crystalline compound was, indeed, a dihydropapaverine was proved by dehydrogenation to papaverine.

Young and Robinson,[11] in a brilliant analysis of the properties of Buck's intermediates, showed that these were incompatible with the above formulation (XXVI to XXVIII). They showed that the product formulated as XXVI was, in fact, an oxazole, XXIX, which is reducible to the amide obtained previously by Pictet and Finkelstein[6] (XX); furthermore, the dihydropapaverine obtained was a purer sample of 3,4–dihydropapaverine than had been previously isolated as an oil. Mixed melting point determinations showed that Robinson's reasoning was correct and that Buck had synthesized, 3,4-dihydropapaverine. The 1,2-dihydroisomer has not been prepared.

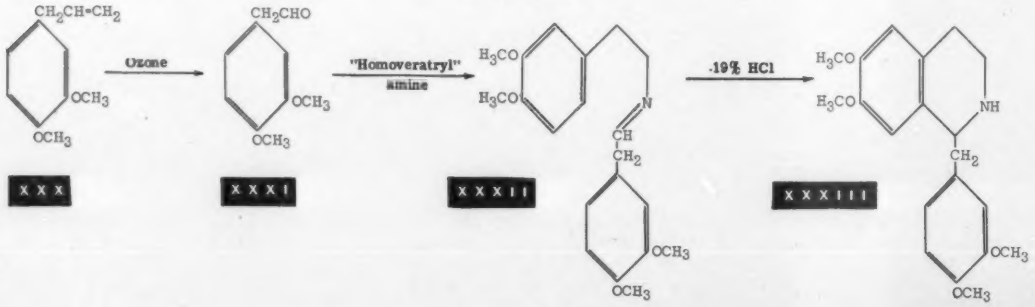
Späth and Berger[12] synthesized papaverine in low yield by a route which is of interest because it employs intermediates which are likely to be the biogenetic precursors of the alkaloid. Their method is shown in chart IV.

Ozonization of eugenol methyl ether (XXX), yielded 3,4–dimethoxyphenyl–acetaldehyde (XXXI). When this biogenetically-feasible intermediate was condensed with β-(3,4-dimethoxyphenyl)-ethyl amine (another substance capable of being available in the plant) the Schiff base XXXII is obtained. Upon heating with hydrochloric acid, this gave a low yield of 1, 2, 3, 4–tetrahydropapaverine (XXXIII), which, as mentioned previously, can be dehydrogenated to papaverine. Though this synthesis has no practical value, it may indicate the biogenetic route (albeit under much milder conditions) of the synthesis of papaverine in the plant.

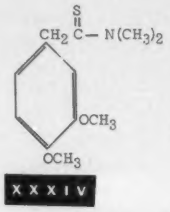
Kindler and Peschke[13] introduced several important practical modifications in the Pictet-Gams synthesis and improved the over-all yield of papaverine. They subjected 3,4–dimethoxy-acetophenone (IX) to the conditions of the Willgerodt reaction (treatment with sulphur and dimethyl amine) and obtained homoveratryl N–dimethyl thio–amide (XXXIV). The latter substance was hydrolyzed with potassium hydroxide to homoveratric acid (XV).

Moreover, these workers found that the acid could be condensed directly with β–(3,4–dimethoxyphenyl)–ethyl amine (XIX) by heating the components in tetralin solution with simultaneous distillation of the water formed in the reaction. This method gives a

Chart IV.



nearly quantitative yield of the Pictet-Finkelstein[6] intermediate XX. The latter was submitted to cyclization with phosphorus oxychloride and dehydrogenation of the resulting 3,4–dihydropapaverine was accomplished by palladium in boiling dihydrophellandrene which is claimed to be an excellent medium for this reaction.

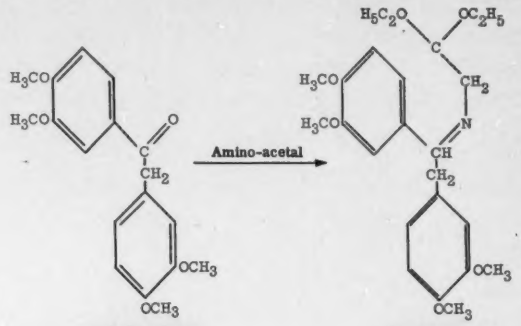


XXXIV

Papaveraldine (1–(3,4–dimethoxybenzoyl) – 6,7 – dimethoxy–isoquinoline) (XXXVI) has been synthesized by Buck, Perkin, and Stevens.[14] Its synthesis is formally a synthesis of papaverine since it has been shown[15] that papaveraldine can be reduced to papaverine through the intermediate carbinol–papaverinol (XXXVII).*

In this synthesis, 3,4–dihydropapaveraldine (XXXV) is obtained by air oxidation of 3,4–dihydropapaverine (XXI) and papaveraldine (XXXVI) is obtained by treatment of the dihydro-compound with alcoholic potassium hydroxide in the presence of air. These transformations and the conversion of papaveraldine to papaverine are summarized in chart V.

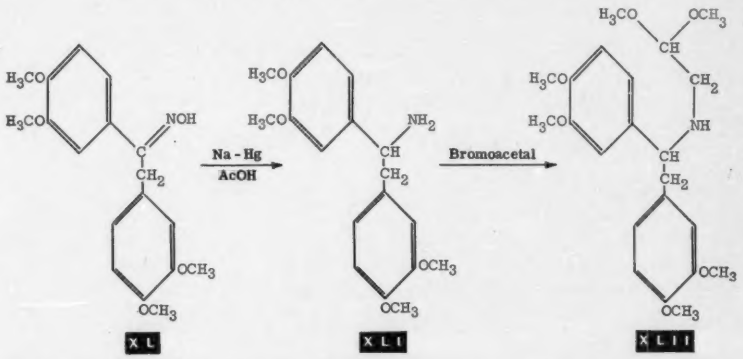
A number of unsuccessful attempts to synthesize papaverine has been recorded in the literature.



XXXVIII XXXIX

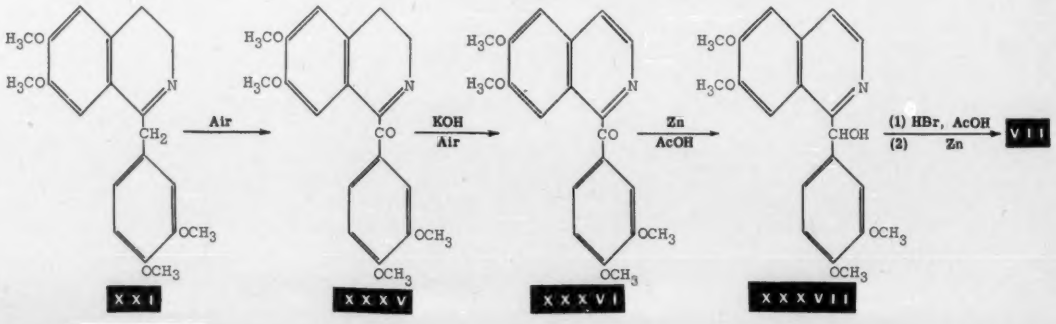
Fritsch[16] condensed amino–acetal with desoxy–veratroin (XXXVIII) and cyclized the product (XXXIX) with concentrated sulphuric acid. Instead of obtaining papaverine, a substance melting 15° higher was formed, the structure of which was not elucidated. Similarly, Allen and Buck,[17] in an attempt to extend Rugheimer and Schön's synthesis of 6,7–dimethoxyisoquinoline,[18] reduced the oxime of desoxyveratroin (XL) with

* This synthesis is recorded here because it is formally a synthesis of papaverine. Obviously, from the practical point of view, 3,4-dihydropapaverine is directly dehydrogenated to papaverine. This synthesis illustrates, however, the great susceptibility of 3,4-dihydropapaverine to air oxidation. For this reason, cyclization of XX to yield XXI and dehydrogenation of XXI are carried out in an inert atmosphere, in plant practice.



XL XLI XLII

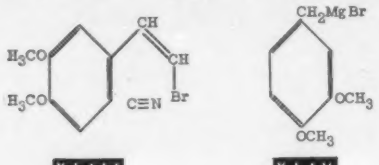
Chart V.



XXI XXXV XXXVI XXXVII VII

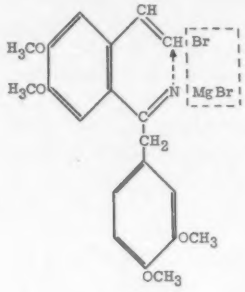
sodium amalgam, condensed the resulting amine XLI with bromoacetal and obtained XLII. Upon attempted cyclization of the latter substance, however, decomposition occurred and no papaverine isolated.

Kefford[19] intended to prepare papaverine by condensation of XLIII with the Grignard reagent from homoveratryl bromide (XLIV). The intermediate



XLIII XLIV

expected, XLV, would then undergo intramolecular cyclization as indicated in the formula. This approach failed, however, when the desired Grignard reagent could not be prepared.



XLV

Syntheses of various substances which can be used as intermediates in the synthesis of papaverine have been described. Many isoquinolines resembling papaverine in structure have been synthesized and, undoubtedly, reactions which have been utilized in the preparation of their intermediates can be applied to the preparation of papaverine intermediates. However, full details of processes for the production of synthetic papaverine currently employed by pharmaceutical manufacturers have not been disclosed.

Certain obvious routes for the synthesis of important papaverine intermediates may now be summarized.

A common precursor for both β-(3,4-dimethoxyphenyl)-ethyl amine and homoveratric acid, is 3,4-dimethoxyphenylacetonitrile (XLVIII). This nitrile can be prepared, for example, as shown in chart VI.

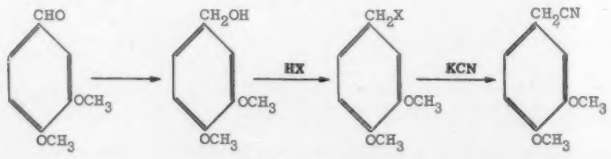
Veratraldehyde (XIII) can be converted to veratryl alcohol (XLVI) by catalytic reduction,[20] by reduction with aluminium isopropylate,[21] or by means of a cross-Canizzaro reaction with formaldehyde.[22] The chloride XLVIIa can be obtained by treatment of the alcohol with hydrogen chloride or thionyl chloride. Similarly, the bromide XLVIIb can be obtained from the alcohol by treatment with hydrogen bromide.[23] Either halide is converted to the nitrile XLVIII by means of potassium cyanide.[21, 24]

Reduction of the nitrile at low or high pressure in the presence of Raney nickel or at low pressure in the presence of noble metal catalysts, yields the required amine XIX. The yield of primary amine has been improved by carrying out the reduction in the presence of ammonia. On the other hand, saponification of XLVIII yields homoveratric acid (XV).[25]

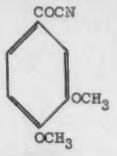
An alternative preparation of 3,4-dimethoxybenzyl chloride (XLVIIa) by chloromethylation of veratrole (VIII) has been described.[24, 26] This method is of practical importance in shortening the number of steps in the papaverine synthesis, and because cheap reagents are utilized in the chloromethylation reaction.

The preparation of β-(3,4-dimethoxyphenyl)-ethyl amine (XIX) in 80 per cent yield by palladium-black reduction of 3,4-dimetroxy-ω-amino-acetophenone (XI), has been reported.[27] The same catalyst effects the reduction of 3,4-dimethoxybenzoyl cyanide (XLIX) to the same amine in 72 per cent yield.[27] The reduction of ω-nitro-styrenes similar to XXII by means of aluminium amalgam,[28] lithium aluminium hydride,[29] or catalytically,[30] to substances analogous to XIX, has been reported. A synthesis of XIX from eugenol methyl ether (XXX) has been devised.[31] Oxidation of the latter with neutral permanganate solution yields the glycol L. The glycol was oxidized with lead tetraacetate to give 3,4-dimethoxyphenylacetaldehyde (XXXI). The oxime of this aldehyde was then reduced to XIX.

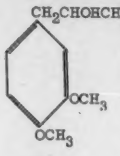
Chart VI.



XIII XLVI XLVII (a) X = Cl (b) X = Br XLVIII



XLIX



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It may be seen from the above discussion, that the synthesis of the key substances in the synthesis of papaverine (XV and XIX) has been rather exhaustively investigated. The methods actually used in production of synthetic papaverine today, combine steps giving the best yields and utilizing the most favourable reaction conditions. Through the improvements listed above, the synthesis of papaverine has been considerably shortened and the yield of the alkaloid substantially increased in the four decades following the first synthesis of this important antispasmodic by Picket and Gams.

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Addendum

A new synthesis of papaverine has been reported independently by Wahl[32] and by Galat.[33] In this approach a 3-carboxy-3, 4-dihydropapaverine (LVI), is the intermediate which Wahl decarboxylated and dehydrogenated in one step, while Galat isolated the intermediate 3,4-dihydropapaverine (XXI) and then dehydrogenated this in the usual way. The yield of the carboxy-amide LIII is higher when LII is treated with ammonia than when LI is treated with the same reagent. Esterification of the free acid LIII followed by phosphorus oxychloride cyclization of the methyl ester LIV yields the 3-carbomethoxy-3,4-dihydropapaverine (LV). Dehydrogenation of this compound is known to give 3-carbomethoxypapaverine.[34] The ester LV was therefore saponified and the free acid obtained (LVI) converted to papaverine either directly or stepwise, as indicated above.

The reactions involved are summarized in chart VII on page 34.

For the sake of completeness, the reviewers are including in this section an interesting report by Eistert,[35] on the synthesis of the key intermediate XX, despite the lack of experimental details in the report. The diazoketone LVII, upon treatment with silver oxide in the presence of β-(3,4-dimethoxyphenyl)-ethyl amine (XIX), evidently forms the amide XX directly. See chart VIII on page 34.

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Chart VII.

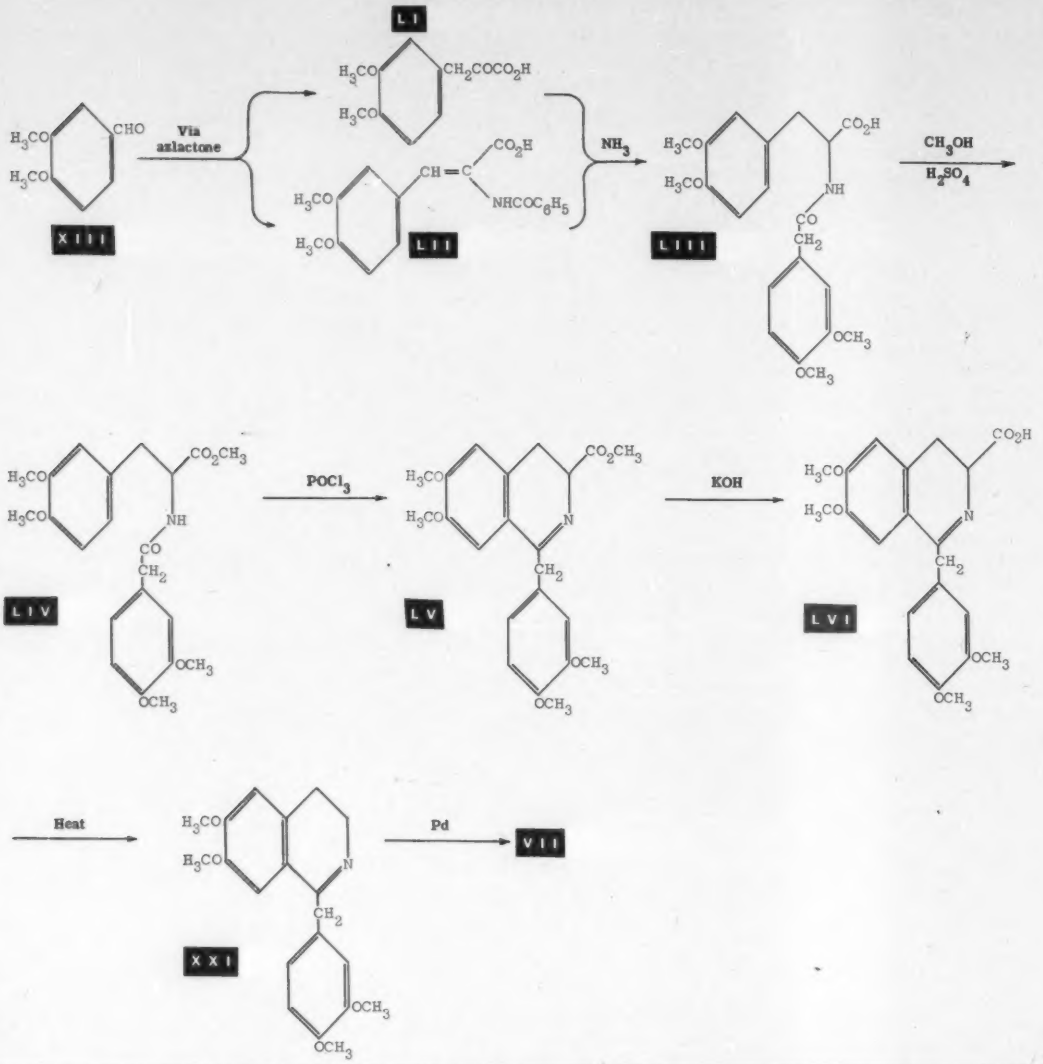
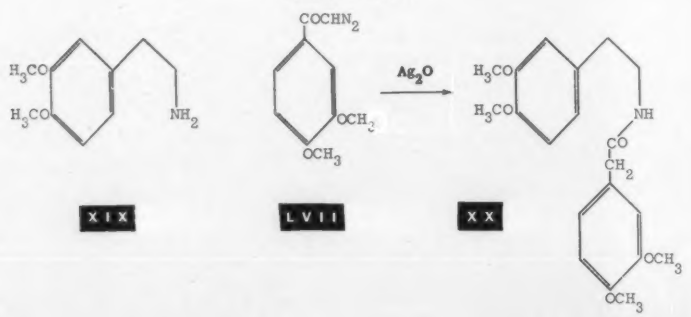


Chart VIII.



Seventh session of the Commission on Narcotic Drugs

The proposed single convention on narcotics, which would replace the existing eight international instruments dating back to 1912, was the major concern of the seventh session of the United Nations Commission on Narcotic Drugs, held at United Nations Headquarters from 15 April to 9 May 1952.

The Commission approved in principle the text of thirteen out of fifty-one proposed articles of the new convention, which had already been discussed by the Commission at its two previous sessions.

Other main narcotics problems on the fourteen-item agenda included that of coca-leaf chewing in Bolivia and Peru; measures to combat the increase in illicit traffic in narcotics since the end of the Second World War; and the control of synthetic narcotic drugs, which have become a dangerous menace to many nations in the past few years.

The Commission, by unanimous vote, elected the following officers for the seventh session: Dr. Oscar Rabasa (Mexico), Chairman; Charles Vaille (France), Vice-Chairman; Dragon Nikolic (Yugoslavia), Rapporteur.

The proposed single convention

The Commission considered the proposed single convention on narcotic drugs. Before the members was the draft prepared by the Secretariat (document E/CN.7/AC.3/3) based on the previous discussions on the matter by the Commission and observations received from governments of six out of the fifteen members of the Commission, as well as those submitted jointly by the Permanent Central Opium Board and the Drug Supervisory Body. During the session the Secretary-General received observations from the World Health Organization, which were also communicated to the Commission.

The Commission decided to proceed to a paragraph-by-paragraph study of the single convention. It also appointed a four-member drafting sub-committee with the task of summing up each day's work and drafting, in stages, a revised text for a later approval of the Commission itself.

The Commission considered on several occasions the extent to which the new convention should be a mere codification, in the narrow meaning of the term, of the existing multilateral treaties for the control of narcotic drugs. There were two points of view on this question. On the one hand, it was argued that the changes to be made in the existing system of international control of narcotics should be limited to those which had been found by experience to be absolutely necessary; on the other, it was contended that the new convention should not necessarily be restricted in scope to a re-enactment of provisions contained in existing treaties, but should, in addition to extending the control to cover the opium poppy, poppy straw, the coca bush and the Indian hemp plant, incorporate such innovations as changed conditions might now warrant, and should also anticipate to some extent possible future developments in the field of narcotic drugs; and the Commission came to the conclusion that there was no fundamental difference between these two views, but merely that the emphasis was different. The Commission did not resolve this theoretical question but considered that each proposed change in the existing control régime should be examined on its particular merits.

After one week of discussions the Commission considered the report of the drafting Committee which had redrafted thirteen of the original fifty-one articles. The draft referred to the text in principle, rather than in a final form. The Secretariat is expected to work out a final version before the Commission's next session.

Among other things the Commission decided that the two main control organs, the Commission itself and the Permanent Central Opium Board, should under the new convention, be known as the "International Narcotics Commission" and the "International Narcotics Board". The new commission would continue to be a functional body under the Economic and Social Council. The composition of the new commission was left for the Economic and Social Council to decide.

The Commission also agreed to include in the new convention a provision which would give effect to certain decisions and recommendations of the Commission without their being subject to approval by the Economic and Social Council. The text of the appropriate draft as adopted by the Commission reads as follows:

> "Except as otherwise expressly provided for in this Convention, the coming into force of each decision or recommendation adopted by the Commission pursuant to the present Convention shall be subject:

"To the right of the Council to approve, set aside or modify the decision or recommendation at its first regular session immediately after the Commission has taken such decision or made such recommendation. If the Council does not exercise this right, the decision or recommendation shall immediately become effective one day after the day on which the Council's session is closed. The Council may waive this right."

In the draft prepared by the Secretariat a provision was made (in article 23) for an International Clearing House to be established under the new convention. This was rejected by the Commission in connexion with the deletion of the provision for governments to supply the Secretariat with names and addresses of authorized importers, exporters and manufacturers of drugs they import, export and manufacture, which are subject to international control.

Finally, the Commission agreed on a number of schedules to appear in the new convention and the categories of drugs to be listed in them. It was agreed that the fourth and last schedule should list the drugs the prohibition of which might be recommended either in the text of the convention itself or later by the Commission. Parties to the new treaty may decide not to act on a recommendation to place a drug in schedule IV, whether such recommendation is written into the instrument itself or made by the Commission after its conclusion, but they would, nevertheless, be bound to prohibit the export of that drug to a country which has accepted the recommendation.

The control of synthetic drugs

The Commission adopted a resolution calling on governments to take strict measures to control synthetic narcotic drugs. The resolution, submitted by France and the United States, notes "that the use of synthetic narcotic drugs is developing rapidly, and that production of these drugs already exceeds that of morphine intended for consumption as such". During the debate of this matter attention was drawn to the fact that increasing laboratory production of synthetic drugs likely to produce addiction had become a major concern. And while control for certain synthetics had been established, a variation in formula might produce a different and uncontrolled drug.

The resolution,

Requests the Secretary-General to draw the attention of governments to the desirability, should they not already have done so, of:

(*a*) Bringing all synthetic narcotic drugs under their national legislation on narcotic drugs as soon as they appear;

(*b*) Acceding without delay to the Protocol of 19 November 1948;

(*c*) Limiting their estimates to medical and scientific requirements;

(*d*) Exercising strict control over the manufacture and therapeutic use of these substances; and

(*e*) Making regulations to ensure that all packages containing a synthetic narcotic drug should be clearly marked with a double red line so that they may be identified by the competent services.

The coca leaf problem

In conformity with the instructions contained in Council resolution 395 D (XIII) of 9 August 1951, the Commission proceeded to examine the problems arising out of the chewing of the coca leaf, taking into consideration all available information. The information referred to was contained in the report of the United Nations Commission of Enquiry on the Coca Leaf, the statement made by the Peruvian representative at the fifth session of the Commission on Narcotic Drugs, the summary records of the Commission's fifth session, the observations of the Commission of Enquiry on the statements made by the Bolivian and Peruvian representatives at that session, and the communications from Bolivia and Peru concerning the report and additional observations of the Commission of Enquiry. This documentary material was supplemented by the report of the WHO Expert Committee on Drugs Liable to Produce Addiction on its third session, and by a special issue of the United Nations *Bulletin on Narcotics* containing a series of articles on the coca leaf written by experts.

The Commission on Narcotic Drugs was assisted in its study of this problem by a Bolivian Government observer whom it had invited to participate in its work. When drafting and discussing the recommendations which it formulated at the conclusion of its work, in conformity with the Council's instructions, the Commission had the advice of a representative of the Technical Assistance Administration and the Technical Assistance Board.

During the discussion it became apparent that the Commission should devote some attention to the nature of coca leaf chewing. Several members of the Commission said that they could not give an opinion on a matter on which there were conflicting scientific opinions. Nevertheless two very different views were expressed. One of these views, based on the conclusions in the report of the Commission of Enquiry, which themselves took into account the definitions given by the World Health Organization in 1950 of addiction-producing and habit-forming drugs, was that coca leaf chewing was not an addiction but a dangerous habit with harmful effects from the point of view of the individual and of the nation. The other view, which was in accordance with the opinion on the nature of chewing expressed in 1952 by the World Health Organization's Expert Committee on Drugs Liable to Produce

Addiction, was to consider it as an addiction. A third point of view was that of the Government of Peru, according to which it was premature to pronounce on the nature of the effects of chewing before new experiments had been made.

Several members questioned, therefore, the competence of the Commission on Narcotic Drugs to deal with this matter. They pointed out that the Commission of Enquiry had concluded in its report that coca leaf chewing was habit-forming only, but did not produce addiction. They felt that this was primarily a social and economic problem outside the scope of the Commission.

Other representatives, considering coca leaf chewing to be harmful both to individuals and to society, declared their belief in the Commission's competence to take a decision on the subject. It was pointed out that even if coca leaf chewing was not a real addiction, the Commission was none the less competent to study any question relating to a raw material which served for the manufacture of narcotics, and that the problem of control of cultivation of the coca bush and that of the surplus production of coca leaf which might go into the illicit traffic and thus contribute to the development of cocaine addiction were within the Commission's province.

At this stage in the discussion, the Commission was reminded that by resolution 395 D (XIII) the Council had formally requested it to submit recommendations on the matter and that there was agreement in principle between the Commission of Enquiry and the Peruvian Government with regard to the experiments to be carried out in certain test areas in order to determine the effects of chewing.

The Commission finally adopted a resolution on the coca leaf problem, the operative part of which recommended that the Economic and Social Council should request the technical assistance services and the specialized agencies, with the help of the Secretariat, to study the possibility of undertaking a field experiment in demonstration areas, within the framework of the existing technical assistance programmes in Bolivia and Peru. The resolution recommended further that the Governments of Bolivia and Peru should take the necessary steps to limit immediately the production of coca leaves to licit consumption and manufacture; and finally urged the Governments of Bolivia and Peru to take effective measures to prevent the introduction into trading channels of coca leaves and cocaine which could form a source of supply for the manufacture or illicit export of narcotic drugs.

Illicit traffic

During the discussion on illicit traffic in narcotic drugs during the year 1951, the Commission examined summaries of illicit transactions and seizures reported by governments, and annual reports on illicit traffic required from parties to the 1931 Convention and paid special attention to the situation in the Far East.

At the end of the discussion on illicit traffic in narcotic drugs, the Commission considered measures to be taken against the illicit traffic in narcotics on merchant ships and aircraft which, members were informed, had increased considerably since the end of the Second World War.

At the Commission's fifth session, the United States representative had introduced a draft resolution on this subject requesting the Secretary-General to compile a list of merchant vessel personnel who had been convicted of crimes involving the smuggling of narcotics since 1946. In addition, the United States representative proposed that governments should take measures to revoke officers' licences and seamen's certificates held by persons who had committed offences against the narcotics laws.

The text of this resolution had been submitted to governments for their comments.

As several members proposed amendments, the resolution, as finally presented during the current session, was a joint text sponsored by Egypt, India, the United States and the United Kingdom.

It asked the Economic and Social Council, in its desire to take all measures possible to combat the illicit traffic which has increased since the war, to request the Secretary-General to compile as soon as may be convenient and thereafter to bring up to date at convenient regular intervals a list of merchant seafarers and members of civil air crews who have been convicted of offences against narcotic laws on or after 1 January 1953, setting out so far as possible the following information:

(*a*) Name (inciuding aliases where appropriate);

(*b*) Nationality;

(*c*) Age;

(*d*) Nature of offence and disposition of the case.

The resolution further asked the Council to instruct the Secretary-General to send the list to the governments of all States with the recommendation of the Council:

(*a*) That they take appropriate measures:

(i) To revoke certificates and licences currently held by merchant seafarers or members of civil air crews so convicted; and

(ii) To withhold the issue to such persons of such licences and certificates, such revocation or withholding of such licences or certificates to be either temporary or permanent as may be appropriate in the circumstances of any particular case, provided that if either course does not accord with national law or usage the government concerned shall send a copy of the list to the competent authorities for such action as the latter

may decide to take under their own domestic laws, or shall have recourse to such other legal measures as may be open to that government to prevent merchant seafarers or members of civil air crews from carrying on their profession;

(*b*) That they send a copy of the list to the maritime and aeronautical unions and companies in their territories for their consideration in connexion with the exercise of their disciplinary functions and any functions which they may exercise in connexion with the engagement of crews.

The Commission further adopted a resolution submitted jointly by Egypt, France, Mexico and the United States, calling upon governments to exercise close international co-operation to control the illicit traffic in narcotics. The resolution asks the Economic and Social Council, in view of the fact that the international illicit traffic in narcotic drugs has increased dangerously, to request the Secretary-General:

(*a*) To advise governments that this baneful trade cannot be combated successfully by national efforts alone, but that international co-operation is of fundamental importance;

(*b*) To urge governments to take immediate steps to establish permanent direct communication between national administrations controlling the illicit traffic; if more than one administration exercises control thereof, the government concerned shall determine the manner in which such communication is to be conducted; and

(*c*) To ask governments to reinforce and alert their preventive organizations as soon as an increase in illicit traffic is discovered within their territories.

The control of heroin in Italy

During the past few years, the Commission was informed, the illicit traffic in diacetylmorphine (heroin) in Italy has risen to dangerous proportions. At its sixth session, the Commission on Narcotic Drugs discussed this problem and asked the Italian authorities to send a report on the question to the Secretary-General.

The Italian Government submitted its report and sent an observer to the Commission's session.

This observer reviewed the measures taken by the Italian authorities to prevent illicit traffic in Italy in the past few years. The production of heroin, he reported, had been suspended indefinitely and further restrictions of its use, even prohibition, were at present under consideration. Penalties for offences against the narcotic law had been increased. He said that Italian authorities, in close co-operation with the international control organs, were doing everything in their power to combat the illicit traffic.

Other business

The Commission also, during its seventh session, took note of reports of governments on the abolition of opium smoking in the Far East, and of a memorandum from the International Criminal Police Commission on the illicit traffic in narcotics in 1951. It recommended that the facilities for the United Nations laboratory, engaged in research on the origin of seized opium, should be enlarged.

The Commission further took note of a report from the Arab League Permanent Anti-Narcotics Bureau, which has been in operation for one year. Several members commended the Bureau for the excellent results in combating illicit traffic in narcotics and limiting cultivation of opium and other plants used in the production of narcotics in the Arab countries.

The Commission took note of the progress report of the Division of Narcotic Drugs and considered matters of priorities for the future work of the Division.

The Commission approved its report to the Economic and Social Council and recommended that its eighth session should be held during the months of April and May next year.

Third session of the World Health Organization Expert Committee on Drugs Liable to Produce Addiction

The Expert Committee on Drugs Liable to Produce Addiction held its third session in Geneva from 7 to 12 January 1952.[1] During this session it examined a series of problems, regarding a certain number of which it submitted formal recommendations.

Ipecopan

The Committee examined a request of the Swiss Government regarding the position, under the provisions of the 1925 Convention, of Ipecopan and its following commercial preparations: Ipecopan malted tablets, Ipecopan solution, Ipecopan malted syrup, Ipesandrine sugar-coated tablets, Ipsandrine solution, Ipesandrine syrup.

The Committee reaffirmed its opinion that Ipecopan powder should not be exempted from the provisions of the 1925 Convention for the reason stated in the report on its second session, but expressed the opinion that such exemption should be granted for the preparations mentioned which contained not more than 0.2 per cent anhydrous morphine compounded with other medicaments. The Committee recommended that its opinions, with respect to Ipecopan and its commercial preparations, should be notified to the Economic and Social Council.

Morphine derivatives

1. *6-Methyldihydromorphine.* The Committee received additional information with respect to this substance which confirmed its previously expressed opinion that it must be classified as an addiction-producing drug.

2. *N-Allylnormorphine.* The Committee received information on the action of N-Allylnormorphine in addicted and previously addicted individuals, leading to the conclusion that liability to its use by addicts is very slight.

3. *Dihydrocodeine and acetyldihydrocodeine.* The Committee previously expressed the opinion that dihydrocodeine and acetyldihydrocodeine are liable to produce addiction. The Committee decided that its opinion regarding these drugs is equally applicable to all their salts and recommended that the Secretary-General of the United Nations should be notified accordingly.

4. *Morpholinylethylmorphine.* The Committee expressed the opinion that morpholinylethylmorphine is not more liable than codeine to produce addiction and is therefore not assimilable to the drugs mentioned in article 1, paragraph 2, subgroup (*a*) of group I of the 1931 Convention, and that it is less readily convertible than codeine to an addiction-producing drug and is, in consequence, assimilable to the drugs mentioned in

[1] Expert advisory panels and committees are an essential part of the machinery of WHO. Their purposes and functions are to provide the Organization with technical advice on particular subjects. The Director-General has authority to establish expert advisory panels and to select and appoint their members, who undertake to contribute by correspondence and without remuneration technical information or reports on developments within their own specialities. They serve in their personal capacity and not as representatives of governments, institutions, organizations, or other bodies. Expert committees are convened to discuss particular subjects; their members are selected by the Director-General from the advisory panels, the choice being governed by the agenda of each session. The selection of members of both expert advisory panels and committees is based primarily upon their ability and technical experience, with due regard to adequate geographical distribution.

The following took part in the third session of the Expert Committee on Drugs Liable to Produce Addiction:

Sir Ram N. Chopra, Professor of Pharmacology; Director, Drug Research Laboratory, Srinagar, Kashmir, India (Vice-Chairman);

Dr. N. B. Eddy, Chief, Section on Analgesics, Division of Chemistry, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md., U.S.A. (Rapporteur);

Dr. H. Fischer, Professeur de Pharmacologie à la Faculté de Médecine de l'Université de Zurich, Switzerland;

Dr. G. Joachimoglu, Professor of Pharmacology; Chairman, Superior Health Council, Ministry of Hygiene, Athens, Greece (Chairman);

Dr. J. La Barre, Professeur de Pharmacologie à la Faculté de Médecine et de Pharmacie de l'Université de Bruxelles, Brussels, Belgium;

Dr. B. Lorenzo-Velázquez, Professor of Pharmacology, Faculty of Medicine, University of Madrid, Spain;

J. R. Nicholls, D.Sc., Deputy Government Chemist, Government Laboratory, London, United Kingdom;

Dr. F. Verzár, Professeur de Physiologie à la Faculté de Médecine de l'Université de Bâle, Switzerland.

L. Atzenwiler, Secretary of the Permanent Central Opium Board, represented the Secretary-General of the United Nations, and

Dr. P. O. Wolff, Chief, Addiction-producing Section, WHO, was the Committee Secretary.

group II of that Convention. The Committee recommended that this opinion should be communicated to the Secretary-General of the United Nations.[2]

5. *Situation regarding diacetylmorphine.* The Committee reiterated its opinion, as expressed in its previous reports, with respect to the continuing gravity of the diacetylmorphine situation. Concerning the request for information circulated to governments by the Director-General of WHO, it is now possible to state that there are fifty member States of WHO who have discontinued, or are willing to discontinue, the medical use of diacetylmorphine. The Committee was gratified by this evidence of changing attitude on the part of the medical profession of many countries in favour of the dispensability of diacetylmorphine inasmuch as at the time of its first session, held in January 1949, so far as was known, there were only twenty-four countries which had discontinued the medical use of the drug.

The Committee was of the opinion that the complete abolition of legally produced diacetylmorphine in the world would greatly facilitate the struggle against illicit use of this substance. The Committee recommended, therefore, that the Executive Board of the World Health Organization should take steps to approach again those States which have not yet answered the first inquiry of the Director-General, or who do not yet consider it possible to discontinue the medical use of diacetylmorphine, asking them whether or not they could do without the drug in the interest of international public health and safety, particularly in view of the fact that the physicians of so many countries find other agents equally satisfactory for symptomatic relief.

Synthetic substances

Synthetic derivatives of morphinan type

The Committee was of the opinion that the régime laid down in the 1931 Convention for the drugs specified in article 1, paragraph 2, group I, should be applied to two synthetic substances of morphinan type and to their salts: 3-hydroxy-N-methylmorphinan and 3-methoxy-N-methylmorphinan. The Committee recommended that this opinion should be communicated to the Secretary-General of the United Nations.

Synthetic derivatives of pethidine type

The Committee expressed an opinion similar to the opinion stated above regarding a substance of "pethidine" type known by the symbol NU-1932.

The Committee stated that as far as the following substances were concerned: pethidine, bemidone, ketobemidone, α-1,3-dimethyl-4 phenyl-4-propionoxypiperidine and β-1,3-dimethyl-4 phenyl-4 propionoxypiperidine, the opinion it expressed in 1949 with respect to their addiction liability and its recommendation to put them under the régime laid down in the 1931 Convention for the drugs specified in article 1, paragraph 2, group I, should be equally applicable to all their salts. The Committee recommended that this opinion should be communicated to the Secretary-General of the United Nations.

Synthetic derivatives of methadone type

The Committee stated that in regard to the following substances: methadone, *iso*-methadone, phenadoxone, 4,4-diphenyl-6-dimethylamino-heptanone-3 and 4,4-diphenyl-6-dimethylamino-3-acetoxyheptane, its opinion expressed in 1949 with respect to their addiction liability and its recommendation to put them under the régime laid down in the 1931 Convention for the drugs specified in article 1, paragraph 2, group I, should be equally applicable to all their salts. The Committee recommended that this opinion should be communicated to the Secretary-General of the United Nations.

Definitions of addiction and habituation

During its second session held in January 1950, the Committee, at the request of the Commission on Narcotic Drugs, propounded definitions of drug addiction, addiction-producing drugs and habit-forming drugs.[3] Taking into consideration the experience since acquired, the Committee reiterated its opinion that a distinction can and must be made between drug addiction and habituation (habit), and between addiction-producing and habit-forming drugs, that the terms are not interchangeable, and that only the expressions "drug addiction" and "addiction-producing drugs" should be used in documentation with respect to substances brought under, or to be brought under, international control. The Committee decided, further, to clarify the distinction between addiction and habituation (habit) by the following statement:

The cycle of administration leading to addiction may begin in legitimate medical use but becomes established as a serious problem through self-administration beyond medical need. In the development of addiction there is an interplay between pharmacological action and the psychological make-up of the individual.

[2] See page 20 of the present issue.

[3] "Drug addiction is a state of periodic or chronic intoxication, detrimental to the individual and to society, produced by the repeated consumption of a drug (natural or synthetic). Its characteristics include:

"1. An overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means;

"2. A tendency to increase the dose;

"3. A psychic (psychological) and sometimes a physical dependence on the effects of the drug".

...

"An addiction-producing drug is one which produces addiction as defined".

...

"A habit-forming drug is one which is or may be taken repeatedly without the production of all the characteristics outlined in the definition of addiction and which is not generally considered to be detrimental to the individual and to society".

There are some drugs, notably morphine and pharmacologically morphine-like substances, whose specific pharmacological action, under individual conditions of time and dose, will always produce compulsive craving, dependence, and addiction in any individual. Addiction will develop sooner in those individuals whose psychological make-up leads them to seek and find escape in the pharmacological action of drugs. Sooner or later there must come a time when the use of the drug cannot be interrupted without significant disturbance, always psychic (psychological) and sometimes physical. With these drugs pharmacological action is paramount, psychological make-up adjuvant. Such drugs cause individual and sociological damage and must be rigidly controlled.

There are other drugs which never produce compulsive craving, yet their pharmacological action is found desirable to some individuals to the point that they readily form a habit of administration, an habituation. Administration of such drugs can be interrupted without significant disturbances. With them psychological make-up is paramount, pharmacological action adjuvant. They cause no sociological damage and do not need rigid control.

There are some drugs whose pharmacological action is intermediate in kind and degree between the two groups already delineated so that compulsive craving, dependence, and addiction can develop in those individuals whose psychological make-up leads them to seek and find an escape in drugs. With these substances psychological make-up is the determining factor but pharmacological action plays a significant role. In some instances individual and sociological damage may develop, but since the incidence of the damage is not general, the type and degree of control of drugs of this group are better left at present to national consideration.

Coca chewing

The report of the Commission of Enquiry on the Coca Leaf clearly shows that coca chewing is detrimental to the individual and to society. The Committee, therefore, was of the opinion that coca chewing comes so closely to the characteristics of addiction as defined by the Committee in 1950[4] that it must be defined and treated as an addiction, in spite of the occasional absence of some of those characteristics.

Cannabis preparations for medical purposes

The question of justification of the use of cannabis preparations for medical purposes was discussed by the Committee. It was of the opinion that cannabis preparations are practically obsolete. So far as it can see, there is no justification for the medical use of cannabis preparations.

Barbiturates

The Committee reviewed the situation with respect to the use and abuse of babiturates throughout the world and the effects of chronic intoxication from these substances. In consequence, the Committee was of the opinion that the barbiturates must be considered drugs liable to produce addiction, dangerous to public health, although differentiation among them with respect to the intensity of this liability cannot be made at this time. The Committee, therefore, was of the opinion that it is advisable to take measures to strengthen the control over these substances on the national level. Such measures might include:

1. Barbiturates should be dispensed only on prescription;

2. Each prescription should specify the number of times it may be refilled or repeated;

3. A careful record should be kept of each prescription.

International non-proprietary names for drugs liable to produce addiction

The Committee discussed ways in which the process of selecting names on the international level would be the most expeditious in regard to drugs liable to produce addiction. The Committee was of the opinion that a common name for a drug liable to produce addiction which may be brought under international control should be selected at the earliest possible moment. The Committee therefore recommended that all agencies concerned be invited to inform WHO as early as possible concerning drugs which may be addiction-producing. The Committee was gratified to learn that the Permanent Central Opium Board and the Drug Supervisory Body employ, in all their documents, the non-proprietary names already selected by WHO for drugs liable to produce addiction, and that the Board is urging all governments to employ these names whenever possible.

Approval of the Expert Committee's opinions and findings

The Executive Board of the World Health Organization, at its ninth session, adopted the following resolution:

"The Executive Board

"1. Adopts the report of the Expert Committee on Drugs Liable to Produce Addiction on its third session;

"2. Thanks the members of the Committee for their work;

"3. Authorizes publication of the report; and

"4. Requests the Director-General again to ask those States which have not yet answered his first inquiry regarding diacetylmorphine, and those which do not yet consider it possible to discontinue its medical use, whether or not they can do without the drug in the interest of international public health and safety, particularly in view of the fact that the physicians of so many countries consider that there are other substances which are satisfactory substitutes for diacetylmorphine."

[4] See above, page 40.

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SCIENTIFIC PUBLICATIONS ON NARCOTIC DRUGS FOR 1951

INTRODUCTION

The following bibliography has been prepared by the Secretariat and includes scientific publications on narcotic drugs which appeared during 1951, as well as a few which appeared earlier but could not, for various technical reasons, be included in the preceding lists, published in No. 3 of Volumes II and III of the *Bulletin on Narcotics*. This bibliography has no claim to be complete, and information regarding books or articles not included in it would be gratefully received by the Division of Narcotic Drugs, Department of Social Affairs, United Nations Secretariat.

The bibliography has been arranged by subject in the following way:

Part I. General and reference works

Part II. Opium poppy, opium and drugs manufactured therefrom

- **A. Opium poppy and opium**
- **B. Morphine**
- **C. Other phenanthrene alkaloids and derivatives of opium (under the Conventions)**
- **D. Other drugs and substances derived from the opium poppy**

Part III.

- **A. The coca leaf**
- **B. Drugs manufactured from the coca leaf**

Part IV. Cannabis and its derivatives

Part V. Synthetic drugs

- **A. General works**
- **B. Pethidine and related compounds**
- **C. Methadone and related compounds**
- **D. Morphinan and morphine synthesis**
- **E. Other synthetic analgesics**

Part VI. Addiction to narcotic drugs

Part VII. Miscellaneous

Under each heading, publications are arranged alphabetically by author. Due to the nature of the sources available to the Secretariat for preparing this bibliography, several of the titles are given in translation only. They are preceded by an asterisk.

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PART V

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